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Search Results -

Term	Documents
(1 AND 2).USPT.	2
(L2 AND L1).USPT.	2

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US Pre-Grant Publication Full-Text Database
JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L3

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Search History

DATE: Monday, September 09, 2002 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=ADJ			
L3	L2 and l1	2	L3
L2	glucocorticoid receptor	932	L2
L1	gr beta or gr alpha	14	L1

END OF SEARCH HISTORY

********** STN Columbus **********

FILE 'JAPIO'
FILE 'BIOSIS'
FILE 'SCISEARCH'
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> s glaucoma#

L1 82458 GLAUCOMA#

=> s l1 and glucocorticoid receptor#

L2 68 L1 AND GLUCOCORTICOID RECEPTOR#

=> s l2 and (glucocorticoid receptor beta or grbeta or gr-beta)

L3 2 L2 AND (GLUCOCORTICOID RECEPTOR BETA OR GRBETA OR GR-BETA)

=> s l2 and ocular hypertension

L4 18 L2 AND OCULAR HYPERTENSION

=> s l3 and l4

L5 0 L3 AND L4

=> dup rem l2

PROCESSING COMPLETED FOR L2
L6 40 DUP REM L2 (28 DUPLICATES REMOVED)

=> dup rem l3

PROCESSING COMPLETED FOR L3
L7 1 DUP REM L3 (1 DUPLICATE REMOVED)

=> dup rem l4

PROCESSING COMPLETED FOR L4
L8 9 DUP REM L4 (9 DUPLICATES REMOVED)

=> d ibib abs l7

L7 ANSWER 1 OF 1 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD DUPLICATE 1
ACCESSION NUMBER: 1998-333347 [29] WPIDS
DOC. NO. CPI: C1998-103395
TITLE: Diagnosing ***glaucoma*** and determining usefulness
of therapeutic agents - by detecting aberrant expression
of beta ***glucocorticoid*** ***receptor*** .
DERWENT CLASS: B04 D16
INVENTOR(S): CLARK, A F; WORDINGER, R J
PATENT ASSIGNEE(S): (CLAR-I) CLARK A F; (WORD-I) WORDINGER R J
COUNTRY COUNT: 23
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9824932	A1	19980611	(199829)*	EN	5

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP MX US
AU 9852617 A 19980629 (199845)
EP 943014 A1 19990922 (199943) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS

PATENT NO	KIND	APPLICATION DATE
WO 9824932	A1	WO 1997-US21054 19971114
AU 9852617	A	AU 1998-52617 19971114
EP 943014	A1	EP 1997-947569 19971114
		WO 1997-US21054 19971114

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9852617	A Based on	WO 9824932
EP 943014	A1 Based on	WO 9824932

PRIORITY APPLN. INFO: US 1996-33227 19961205
AN 1998-333347 [29] WPIDS
AB WO 9824932 A UPAB: 19980722
Diagnosing ***glaucoma*** comprises either:
(i) detecting aberrant ***glucocorticoid*** ***receptor*** (***GR***) ***beta*** expression or defects in a GR gene which
encodes ***GR*** ***beta*** ,
(ii) detecting genetic changes in the GR gene leading to altered
GR ***beta*** expression, or
(iii) detecting genetic changes outside the GR gene which lead to
altered ***GR*** ***beta*** expression.
Also claimed is a method for determining whether an agent is useful
for treating ***glaucoma*** by determining whether it interacts with
GR ***beta*** or alters the expression of ***GR***
beta .
USE - Cultured human trabecular meshwork cell lines derived from
glaucomatous donors express mRNA for both on alternate splice form of the
human ***glucocorticoid*** ***receptor*** (***GR***
beta), as well as the normal glucocorticiod receptor (GR alpha),
whereas normal tm cell lines only express mRNA for GR alpha . Determining
that an individual abnormally expresses ***GR*** ***beta*** in
their trabecular meshwork or other tissues can lead to a diagnosis of
glaucoma . Agents that have therapeutic value for treating
glaucoma can be determined by using ligand binding assays or
GR ***beta*** functional assays.
Dwg.0/0

=> d ibib abs l8 1-9

L8 ANSWER 1 OF 9 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-491060 [43] WPIDS
DOC. NO. CPI: C2000-147602
TITLE: Diagnosis, prognosis and treatment of ***glaucoma*** ,
based on detecting specific polymorphisms in the promoter
of the trabecular meshwork inducible
glucocorticoid ***receptor*** gene.
DERWENT CLASS: B04 D16
INVENTOR(S): CHEN, H; CHEN, P; NGUYEN, T D; POLANSKY, J R
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000042220	A1	20000720	(200043)*	EN	121

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

APPLICATION DETAILS

PATENT NO	KIND	APPLICATION DATE
WO 2000042220	A1	WO 2000-US559 20000111

PRIORITY APPLN. INFO: US 1999-306828 19990507, US 1999-227881 19990111
AN 2000-491060 [43] WPIDS
AB WO 200042220 A UPAB: 20000907
NOVELTY - A method for the diagnosis, prognosis and treatment of
glaucoma , based on detecting specific polymorphisms in the
promoter of the trabecular meshwork inducible ***glucocorticoid***
receptor gene, is new.
DETAILED DESCRIPTION - Diagnosis, or prognosis, of ***glaucoma***
comprises incubating a marker nucleic acid (I) that hybridizes
specifically with a polynucleotide linked to a TIGR (trabecular meshwork
inducible ***glucocorticoid*** ***receptor***) promoter with
complementary nucleic acid (II) present in a patient's cell or body fluid
sample. (I) and (II) hybridize and a polymorphism is detected that is:
(i) predictive of a mutation affecting TIGR response; and
(ii) diagnostic (prognostic) of ***glaucoma***

INDEPENDENT CLAIMS are also included for the following:
(a) a similar method for diagnosing sensitivity to steroids,
(b) a nucleic acid (III) that comprises any of the sequences (N1)
(5300 bp (base pairs)), (N3) (6169 bp), (N4) (926 bp), (N5) (2099 bp) or
(N24) (1548 bp);
(c) a recombinant DNA (IIIa) that hybridizes specifically to the
sequences of (b);
(d) a pure molecule (IV) that binds to (III);
(e) a pure molecule (IVa) that binds to any of about 40 specified
nucleic acids that include a cis-element;
(f) a method for the treatment of ***glaucoma*** by administering
an agent that binds a cis-element present in (N1),
(g) a nucleic acid (IIIb) that is (a region of) (N33) which comprises
the sequence CAAACAGACTTCCGGAAGGT,
(h) a nucleic acid (IIIc) that hybridizes specifically to (IIIb),
(i) a vector or cell containing (IIIb),
(j) a method for detecting the characteristic TIGRmt11 sequence by
hybridization to labeled (IIIb), for detecting increased susceptibility to
glaucoma , progressive ocular hypertensive disease or steroid
sensitivity;
(k) a kit for method OF (j) containing labeled (IIIb) and system for
detecting hybridization;
(l) a nucleic acid (IIId) that is (N1), (N3), (N2) (5304 bp) or (N34)
(5271 bp) or any of their fragments that contain a functional regulatory
sequence;
(m) cells or vectors containing (IIId),

(n) a method for detecting the TIGRmt11 sequence variant by amplification,
(o) kit for method of (n) containing amplification primers and enzyme,
(p) a method for detecting a polymorphism in the 5'-flanking region of TIGR by amplification with specific primers (sequences reproduced in specification),
(q) the nucleic acids (N37) (283 bp) and (N38) (227 bp), sequences 95% identical with them or their variants,
(r) recombinant nucleic acids, vectors and cells containing the sequences of (q),
(s) identification of a protein or compound that binds to, and modifies expression of, TIGR from ability to bind to (N37), (N38) or their variants, or to regions of (N3) or (N34),
(t) a method for identifying a compound that modulates the binding reaction in (s), and
(u) a method for identifying compounds that modulate steroid induction of a TIGR gene.
ACTIVITY - Antiglaucoma; ophthalmic.
No data given.
MECHANISM OF ACTION - Modulation of expression of the TIGR gene.
USE - The method is used for diagnosis and prognosis of glaucoma (of all types), steroid sensitivity and progressive ocular hypertension that leads to loss of vision. Also glaucoma can be treated by administering an agent that binds to cis-acting elements within the TIGR promoter. The TIGR promoter (or other regulatory regions) can be used to express homologous or heterologous genes, particularly for tissue-specific expression of therapeutic transgenes for treating glaucoma, also to generate transgenic animals and in screening for compounds (specific modulators) with diagnostic or therapeutic potential. Fragments of the TIGR sequence can be used as amplification primers or probes, e.g. for isolating related sequences in non-human animals.
Dwg.0/9

L8 ANSWER 2 OF 9 MEDLINE
ACCESSION NUMBER: 2000414284 MEDLINE
DOCUMENT NUMBER: 20388270
TITLE: [Hormonal changes in male patients with primary open angle ***glaucoma***]. Ocena zmian hormonalnych u mezczyzn chorych na jaskre prosta otwartego kata przesaczania.
AUTHOR: Nowak M.[, Swietochowska E, Jochan K, Buntner B
CORPORATE SOURCE: Zakladu Patofizjologii i Endokrynologii Slaskiej AM w Zabrzu.
SOURCE: KLINIKA OCZNA, (2000) 102 (2) 103-8.
Journal code: KWC. ISSN: 0023-2157.
PUB. COUNTRY: Poland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Polish
ENTRY MONTH: 200011
ENTRY WEEK: 20001101
AB INTRODUCTION: Primary open angle ***glaucoma*** (POAG) is the most common type of ***glaucoma*** , pathogenesis of which is not completely known. Several clinical studies show that glucocorticoid hormones may be implicated in the pathogenesis of POAG and ***ocular*** ***hypertension*** ***Glucocorticoid*** ***receptors*** have been identified in human outflow tissue of the eye. AIMS: The purpose of this study, therefore, was to evaluate the serum concentration of total cortisol (TF), total testosterone (TT), free testosterone (FT), FSH (follitropin), LH (lutropin), ACTH (adrenocorticotropin), SHBG (sex hormone-binding globulin), DHEA-SO4 (dehydroepiandrosterone sulfate) as well as free cortisol (UFF) and 17-OHCS in 24 hours urinary samples in patients treated because of POAG. PATIENTS AND METHODS: Studies were performed in the group of 30 male patients, aged 55 +/- 13 years, treated because of ***glaucoma*** for more than two years. Serum and urinary concentration of hormones were studied using RIA methods (DPC). RESULTS: The serum concentration of TF (652.03 +/- 315.43 nmol/l), UFF (248.75 +/- 99.39 nmol/l) and 17-OHCS (5.47 +/- 2.64 mg/24 h) in urine was increased compared with control group. There was not significant difference in concentration of pituitary-gonadal axis hormones in glaucomatous and control groups of patients. CONCLUSION: The results could point to the fact that changes in the endocrine system are one of the factors involved in the pathogenesis of POAG. We conclude that an elevated level of cortisol, free cortisol and its metabolites is closely related to the POAG.

L8 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:274116 BIOSIS
DOCUMENT NUMBER: PREV199900274116
TITLE: Glucocorticoid target receptors and isozymes of 11B-hydroxysteroid dehydrogenase in normal and glaucomatous human eyes.
AUTHOR(S): Stokes, J. D.; Andrew, R. (1); Seckl, J. R. (1); O'Brien, C.
CORPORATE SOURCE: (1) Dept. of Medicine, Western General Hospital, University of Edinburgh, Edinburgh UK
SOURCE: IOVS, (March 15, 1999) Vol. 40, No. 4, pp. S669.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology Fort Lauderdale, Florida, USA May 9-14, 1999 Association for Research in Vision and Opthalmology
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 4 OF 9 MEDLINE
ACCESSION NUMBER: 1999364864 MEDLINE
DOCUMENT NUMBER: 99364864
TITLE: Effects of glucocorticoids on the trabecular meshwork: towards a better understanding of ***glaucoma*** .
AUTHOR: Wordinger R J; Clark A F
CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of North Texas, Health Science Center, Fort Worth 76107, USA. rwording@hsc.unt.edu
SOURCE: PROGRESS IN RETINAL AND EYE RESEARCH, (1999 Sep) 18 (5) 629-67. Ref: 224
Journal code: C2P. ISSN: 1350-9462.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW) (REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY WEEK: 19991102
AB Glucocorticoid effects on the human trabecular meshwork can be used as a model system in which to study glaucomatous damage to the trabecular meshwork. One of the most important risk factors for ***glaucoma*** is an elevated intraocular pressure. The administration of glucocorticoids also can cause elevated intraocular pressure in some individuals. In addition, there is suggestive evidence linking glucocorticoids with the development of ***glaucoma*** . Glucocorticoids cause multiple effects on the human trabecular meshwork including changes in extracellular matrix metabolism, organisation of the cytoskeleton, and changes in gene expression and cell function. New discoveries on the molecular mechanisms of ***glucocorticoid*** ***receptor*** action provide new opportunities to study the possible role of this receptor in the development of ***glaucoma*** . For example, alternate spliced forms of the ***glucocorticoid*** ***receptor*** , ***glucocorticoid*** ***receptor*** response element half-sites, numerous modulatory factors, and direct effects of nuclear transcription factors have been recently described. Other recent information has shown that the new ***glaucoma*** gene (GLC1A/myocilin) is induced in the human trabecular meshwork by glucocorticoids. Although the exact function of myocilin is currently unknown, it offers the opportunity to dissect the molecular pathways regulating aqueous humor outflow. Future challenges include determining (1) which glucocorticoid effects in the human trabecular meshwork are responsible for elevated intraocular pressure, and (2) the significance of these findings to the development of ***glaucoma*** .

L8 ANSWER 5 OF 9 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
ACCESSION NUMBER: 1997:303241 BIOSIS
DOCUMENT NUMBER: PREV199799602444
TITLE: PCR-SSCP analysis of the glucocorticoid-responsive element of the atrial natriuretic peptide gene familial primary open-angle ***glaucoma*** .
AUTHOR(S): Richardson, Kimberley A.; Tunny, Terry J. (1); Clark, Charles V.
CORPORATE SOURCE: (1) Univ. Dep. Med., Greenslopes Hosp., Brisbane, QLD 4120 Australia
SOURCE: Clinical and Experimental Pharmacology and Physiology, (1997) Vol. 24, No. 6, pp. 427-429. ISSN: 0305-1870.
DOCUMENT TYPE: Article
LANGUAGE: English
AB 1. Familial primary open-angle ***glaucoma*** (POAG) is a heterogeneous disease of unknown aetiology and the elucidation of the underlying genetic mechanisms contributing to phenotypic expression will be essential if earlier diagnosis of at-risk individuals and more specific medical treatment can be achieved. In a significant percentage of patients with POAG, intraocular pressure increases in response to topical ocular glucocorticoids. 2. Atrial natriuretic peptide (ANP) assists in the regulation of intraocular pressure levels and binding of the

glucocorticoid ***receptor*** dimer to the
glucocorticoid-responsive element in intron 2 of the ANP gene has been
shown to increase ANP mRNA levels in vitro. We amplified and examined this
sequence in the ANP gene by PCR-SSCP analysis in 100 patients with
familial POAG and in 60 normal control subjects. No base alterations in
the amplified product were found. 3. Thus, the present study found no
evidence for an alteration in the sequence of the glucocorticoid-
responsive element of the ANP gene that could alter ANP gene transcription
in patients with familial POAG. The mechanism responsible for the increase
in intraocular pressure levels in response to glucocorticoids is most
likely independent of the glucocorticoid-responsive element in the ANP
gene.

L8 ANSWER 6 OF 9 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 96:286937 SCISEARCH
THE GENUINE ARTICLE: UD853
TITLE: INHIBITION OF DEXAMETHASONE-INDUCED CYTOSKELETAL CHANGES
IN CULTURED HUMAN TRABECULAR MESHWORK CELLS BY TETRAHYDROCORTISOL
AUTHOR: CLARK A F (Reprint); LANE D; WILSON K; MIGGANS S T; MCCARTNEY M D
CORPORATE SOURCE: ALCON LABS INC, GLAUCOMA RES R241, 6201 S FREEWAY, FT WORTH, TX, 76134 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, (APR 1996)
Vol. 37, No. 5, pp. 805-813.
ISSN: 0146-0404.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 47
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Purpose. To determine the cellular mechanism of action of the
intraocular pressure (IOP) lowering steroid tetrahydrocortisol (THF).
Methods. Tetrahydrocortisol was evaluated for glucocorticoid antagonist
activity using in vitro and in vivo assays. Systemically administered THF
was evaluated for its ability to inhibit dexamethasone-induced body weight
loss and systemic hypertension in rats. In vitro receptor antagonism was
tested using the supernatant fraction of IM9 cells as the source of
soluble ***glucocorticoid*** ***receptor*** in H-3-dexamethasone
displacement binding assays. In addition, six different primary human
trabecular meshwork (TM) cell lines were cultured for 0 to 14 days in the
absence or presence of dexamethasone (10(-7) M) and/or THF (10(-6) to
10(-6) M). The effects of these steroids on the TM cytoskeleton were
determined by epifluorescent microscopy and by transmission electron
microscopy.
Results. Tetrahydrocortisol was unable to inhibit the dexamethasone
(DEX)-induced systemic hypertension and decrease in body mass in rats and
was unable to displace H-3-DEX from the soluble human
glucocorticoid ***receptor***. However, THF inhibited the
DEX-induced formation of cross-linked actin networks in cultured human TM
cells in a progressive and dose-dependent manner (IC50 = 5.7 x 10(-7) M).
Dexamethasone caused changes in the TM cell microtubules that were
reversed partially by concomitant treatment with THF. Tetrahydrocortisol
alone appeared to increase microfilament bundling in TM cells.
Conclusions. Tetrahydrocortisol was not a glucocorticoid antagonist at
the level of the classical ***glucocorticoid*** ***receptor*** and
did not appear to antagonize systemically mediated glucocorticoid activity
in the rat, Tetrahydrocortisol inhibited DEX-induced changes in the TM
microfilaments and microtubules. These results may explain partially the
IOP lowering activity of THF because glucocorticoid-mediated changes in
the TM cytoskeleton have been proposed to be involved in the generation of
ocular ***hypertension***.

L8 ANSWER 7 OF 9 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 94131755 MEDLINE
DOCUMENT NUMBER: 94131755
TITLE: Glucocorticoid-induced formation of cross-linked actin
networks in cultured human trabecular meshwork cells.
AUTHOR: Clark A F, Wilson K, McCartney M D, Miggans S T, Kunkle M, Howe W
CORPORATE SOURCE: Alcon Laboratories, Inc., Fort Worth, Texas 76134.
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1994 Jan)
35 (1) 281-94.
Journal code: GWI. ISSN: 0146-0404.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
AB PURPOSE. To determine the effects of glucocorticoid treatment on the
microfilament structure of cultured human trabecular meshwork cells.
Topical or systemic administration of glucocorticoids can lead to the
development of ***ocular*** ***hypertension*** and to the
development of vision loss, which is clinically similar to primary open
angle ***glaucoma***. However, the mechanism(s) by which
glucocorticoids cause ***ocular*** ***hypertension*** is not well
defined. Alterations in the trabecular meshwork, the site of drainage of
aqueous humor from the eye, have been linked to the development of
ocular ***hypertension***.
METHODS. Human trabecular meshwork cells were cultured in the presence and absence of glucocorticoids for 0
to 21 days. The microfilament organization of the cultured trabecular
meshwork cells was examined by epifluorescent and transmission electron
microscopy. RESULTS. Glucocorticoids caused a progressive change in the
organization of microfilaments in the trabecular meshwork cells, but not
in other cultured ocular cells. By fluorescence microscopic analysis, the
actin stress fibers found in control trabecular meshwork cells were
reorganized on treatment with glucocorticoids into cross-linked actin
networks that resembled geodesic-dome-like polygonal lattices. The
cross-linked actin networks were reversible on withdrawal of the
glucocorticoid treatment. Dose-response data for dexamethasone, relative
ranking of activity with glucocorticoid potency, and partial inhibition
with glucocorticoid antagonists all suggest the involvement of the
trabecular meshwork ***glucocorticoid*** ***receptor*** in
cross-linked actin network formation. The reorganization of the trabecular
meshwork cytoskeleton alters cell function because glucocorticoid
treatment of cultured trabecular meshwork cells also inhibited trabecular
meshwork cell migration and proliferation.
CONCLUSION. The steroid-induced
alteration in trabecular meshwork cytoskeleton may be an important factor
in the development of steroid-induced ***ocular***
hypertension and may play a role in the ***ocular***
hypertension associated with primary open angle ***glaucoma***

L8 ANSWER 8 OF 9 MEDLINE
DUPLICATE 3
ACCESSION NUMBER: 91201034 MEDLINE
DOCUMENT NUMBER: 91201034
TITLE: Increased plasma noncortisol glucocorticoid activity in
open-angle ***glaucoma*** [published erratum appears in
Invest Ophthalmol Vis Sci 1991 Jul;32(8):2440].
AUTHOR: McCarty G R, Schwartz B
CORPORATE SOURCE: Department of Ophthalmology, New England Medical Centre
Hospitals, Boston, Massachusetts 02111.
CONTRACT NUMBER: EY00024 (NEI)
EY07045 (NEI)
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1991 Apr)
32 (5) 1600-8.
Journal code: GWI. ISSN: 0146-0404.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
AB Total biologic plasma glucocorticoid activity of normal, ocular
hypertensive, and open-angle ***glaucoma*** patients was compared
using a ***glucocorticoid*** ***receptor*** -based competitive
binding assay. Multiple linear-regression analysis was used to adjust for
the effects of significant ocular and nonocular variables, including
therapy for ***glaucoma***. The ***glaucoma*** patients had
significantly greater plasma glucocorticoid activities than did normal
subjects. A comparison of receptor-based assay values to values obtained
with a cortisol radioimmunoassay showed that significant amounts of
biologic glucocorticoid activity in the plasma of the ***glaucoma***
patients could not be explained by cortisol alone. In the normal and
ocular hypertensive groups, however, virtually all of the plasma
glucocorticoid activity could be accounted for by cortisol. These results
suggest that in open-angle ***glaucoma*** patients, noncortisol
glucocorticoids are responsible for elevating biologic plasma
glucocorticoid activity. Thus, open-angle ***glaucoma*** may be
associated with a disturbance of the hypothalamic-pituitary-adrenal axis
that produces increased plasma levels of both cortisol and other

noncortisol glucocorticoids

L8 ANSWER 9 OF 9 MEDLINE
DUPLICATE 4
ACCESSION NUMBER: 84017537 MEDLINE
DOCUMENT NUMBER: 84017537
TITLE: Potentiation of glucocorticoid activity by 5
beta-dihydrocortisol: its role in ***glaucoma***.
AUTHOR: Weinstein B I; Gordon G G; Southren A L
CONTRACT NUMBER: EY 01313 (NEI)
SOURCE: SCIENCE, (1983 Oct 14) 222 (4620) 172-3.
Journal code: UJ7. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals, Cancer Journals
ENTRY MONTH: 198401
AB 5 beta-Dihydrocortisol potentiated the threshold level (the smallest dose
producing a measurable effect) of topically applied cortisol (0.02
percent) and dexamethasone (0.003 percent) in causing nuclear
translocation of the cytosolic ***glucocorticoid*** ***receptor*** in rabbit iris-ciliary body tissue. 5 beta-Dihydrocortisol accumulates in
cells cultured from trabecular meshwork specimens from patients with
primary open-angle ***glaucoma***, but not in similar cells derived
from nonglaucomatous patients. In view of the sensitivity of patients with
primary open-angle ***glaucoma*** to the effects of glucocorticoids in
raising intraocular pressure, this potentiation may be responsible for the
steroid sensitivity and for the ***ocular*** ***hypertension*** seen in this disorder.

=> d ibib abs l6 1-40

L6 ANSWER 1 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-491060 [43] WPIDS
DOC. NO. CPI: C2000-147602
TITLE: Diagnosis, prognosis and treatment of ***glaucoma***,
based on detecting specific polymorphisms in the promoter
of the trabecular meshwork inducible ***glucocorticoid*** ***receptor*** gene.
DERWENT CLASS: B04 D16
INVENTOR(S): CHEN, H; CHEN, P; NGUYEN, T D; POLANSKY, J R
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000042220	A1	20000720	(200043)*	EN	121

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

APPLICATION DETAILS

PATENT NO	KIND	APPLICATION DATE
WO 2000042220	A1	WO 2000-US559 20000111

PRIORITY APPLN. INFO: US 1999-306828 19990507; US 1999-227881 19990111
AN 2000-491060 [43] WPIDS
AB WO 200042220 A UPAB: 20000907
NOVELTY - A method for the diagnosis, prognosis and treatment of ***glaucoma***, based on detecting specific polymorphisms in the
promoter of the trabecular meshwork inducible ***glucocorticoid*** ***receptor*** gene, is new.
DETAILED DESCRIPTION - Diagnosis, or prognosis, of ***glaucoma*** comprises incubating a marker nucleic acid (I) that hybridizes
specifically with a polynucleotide linked to a TIGR (trabecular meshwork
inducible ***glucocorticoid*** ***receptor***) promoter with
complementary nucleic acid (II) present in a patient's cell or body fluid
sample. (I) and (II) hybridize and a polymorphism is detected that is:
(i) predictive of a mutation affecting TIGR response, and
(ii) diagnostic (prognostic) of ***glaucoma***.

INDEPENDENT CLAIMS are also included for the following.
(a) a similar method for diagnosing sensitivity to steroids;
(b) a nucleic acid (III) that comprises any of the sequences (N1) (5300 bp (base pairs)), (N3) (6169 bp), (N4) (926 bp), (N5) (2099 bp) or (N24) (1548 bp);
(c) a recombinant DNA (IIIa) that hybridizes specifically to the sequences of (b);
(d) a pure molecule (IV) that binds to (III);
(e) a pure molecule (IVa) that binds to any of about 40 specified nucleic acids that include a cis-element;
(f) a method for the treatment of ***glaucoma*** by administering an agent that binds a cis-element present in (N1);
(g) a nucleic acid (IIIb) that is (a region of) (N33) which comprises the sequence CAAACAGACTTCCGGAAGGT;
(h) a nucleic acid (IIIc) that hybridizes specifically to (IIIb);
(i) a vector or cell containing (IIIb);
(j) a method for detecting the characteristic TIGRmt11 sequence by hybridization to labeled (IIIb), for detecting increased susceptibility to ***glaucoma***, progressive ocular hypertensive disease or steroid sensitivity;
(k) a kit for method OF (j) containing labeled (IIIb) and system for detecting hybridization;
(l) a nucleic acid (IIId) that is (N1), (N3), (N2) (5304 bp) or (N34) (5271 bp) or any of their fragments that contain a functional regulatory sequence;
(m) cells or vectors containing (IIId);
(n) a method for detecting the TIGRmt11 sequence variant by amplification;
(o) kit for method of (n) containing amplification primers and enzyme;
(p) a method for detecting a polymorphism in the 5'-flanking region of TIGR by amplification with specific primers (sequences reproduced in specification);
(q) the nucleic acids (N37) (283 bp) and (N38) (227 bp), sequences 95% identical with them or their variants,
(r) recombinant nucleic acids, vectors and cells containing the sequences of (q),
(s) identification of a protein or compound that binds to, and modifies expression of, TIGR from ability to bind to (N37), (N38) or their variants, or to regions of (N3) or (N34),
(t) a method for identifying a compound that modulates the binding reaction in (s), and
(u) a method for identifying compounds that modulate steroid induction of a TIGR gene.
ACTIVITY - Antiglaucoma; ophthalmic. No data given.
MECHANISM OF ACTION - Modulation of expression of the TIGR gene.
USE - The method is used for diagnosis and prognosis of glaucoma (of all types), steroid sensitivity and progressive ocular hypertension that leads to loss of vision. Also glaucoma can be treated by administering an agent that binds to cis-acting elements within the TIGR promoter. The TIGR promoter (or other regulatory regions) can be used to express homologous or heterologous genes, particularly for tissue-specific expression of therapeutic transgenes for treating glaucoma, also to generate transgenic animals and in screening for compounds (specific modulators) with diagnostic or therapeutic potential. Fragments of the TIGR sequence can be used as amplification primers or probes, e.g. for isolating related sequences in non-human animals.
Dwg.0/9

L6 ANSWER 2 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-205642 [18] WPIDS
DOC. NO. CPI: C2000-063422
TITLE: Novel glucocorticoid and thyroid hormone receptor ligands
useful for treating diabetes, inflammation and obesity.
DERWENT CLASS: B05
INVENTOR(S): APELQVIST, T; GOEDE, P; HOLMGREN, E
PATENT ASSIGNEE(S): (KARO-N) KAROBIO AB; (KARO-N) KARO BIO AB
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000007972	A1	20000217	(200018)*	EN	54

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9951881 A 20000228 (200030)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DATE
WO 2000007972	A1	WO 1999-IB1447 19990804
AU 9951881	A	AU 1999-51881 19990804

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9951881	A Based on	WO 200007972

PRIORITY APPLN. INFO: GB 1998-16935 19980805
AN 2000-205642 [18] WPIDS
AB WO 200007972 A UPAB: 20000412
NOVELTY - Novel liver-selective ***glucocorticoid*** ***receptor*** antagonists are useful for the treatment of metabolic disorders.
DETAILED DESCRIPTION - Diphenyl compounds of formula (I) and their salts and stereoisomers are new:
R1 = aliphatic hydrocarbyl, aromatic hydrocarbyl, carboxylic acid or its ester, alkenyl carboxylic acid or its ester, OH, halo or CN;
R2, R3 = H, halo, 1-4C alkyl or 3-5C cycloalkyl; provided that at least one is not H;
X = CO or CH2;
R4 = aliphatic, aromatic, or heteroaromatic;
R5 = halo, 1-4C alkyl or 3-5C cycloalkyl;
Y = OH, OMe, amino or alkylamino, and n = 0-4.
ACTIVITY - Antidiabetic, Antiinflammatory, Endocrine-Gen.; Antiarteriosclerotic; Antiarrhythmic; Antidepressant; Osetopathic; Antilipemic; Anorectic; Ophthalmological.
MECHANISM OF ACTION - ***Glucocorticoid*** - ***Receptor*** -Antagonist; Thyroid-Receptor-Antagonist.
USE - (I) are useful for preventing, inhibiting or treating diseases associated with a metabolism dysfunction or which is dependent on the expression of a ***glucocorticoid*** ***receptor*** regulated gene such as diabetes, Cushing's syndrome, inflammation, hypercholesterolemia, obesity, skin disorders, ***glaucoma*** or other endocrine disorders related to thyroid hormone (claimed). (I) are also useful for treating atherosclerosis, cardiac arrhythmias, depression, osteoporosis, hypothyroidism, thyroid cancer as well as ***glaucoma*** and congestive heart failure.
ADVANTAGE - (I) are preferably liver selective.
Dwg.0/0

L6 ANSWER 3 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000276535 EMBASE
TITLE: Assessment of therapeutic index of inhaled steroids.
AUTHOR: Israel E.
CORPORATE SOURCE: E. Israel, Div. Pulmonary Critical Care Med., Brigham Womens Hospital, Harvard Medical School, Boston, MA 02115, United States
SOURCE: Lancet, (12 Aug 2000) 356/9229 (527-528).
Refs: 4
ISSN: 0140-6736 CODEN: LANCAO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal, Note
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English

L6 ANSWER 4 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000402241 BIOSIS
DOCUMENT NUMBER: PREV200000402241
TITLE: The genetics of open-angle ***glaucoma***. The story of GLC1A and myocilin
AUTHOR(S): Alward, Wallace L. M. (1)
CORPORATE SOURCE: (1) Department of Ophthalmology, University of Iowa College of Medicine, 200 Hawkins Drive, Iowa City, IA, 52242-1091 USA
SOURCE: Eye (London), (June, 2000) Vol. 14, No. 3B, pp. 429-436. print.
ISSN: 0950-222X
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A linkage analysis study was performed on a single large family with juvenile-onset primary open-angle ***glaucoma*** (POAG). This led to the recognition that there was a region of chromosome 1q that harboured a gene for juvenile-onset POAG. This chromosomal site was called GLC1A. It was discovered that a gene that produces the protein myocilin resides within this interval and that mutations in myocilin caused most cases of autosomal dominant juvenile-onset POAG. More importantly myocilin mutations also cause up to 4.6% of cases of adult-onset POAG. The prevalence of myocilin mutations is similar regardless of race or geographic location. There are widely variable ***glaucoma*** phenotypes depending on the specific mutation in myocilin. Myocilin is expressed in multiple tissues throughout the eye and in many other organs. In the trabecular meshwork the production of myocilin can be induced by the application of topical corticosteroids. The exact function of myocilin in health and disease remains a mystery.

L6 ANSWER 5 OF 40 MEDLINE
ACCESSION NUMBER: 2000414284 MEDLINE
DOCUMENT NUMBER: 20388270
TITLE: [Hormonal changes in male patients with primary open angle ***glaucoma***].
Ocena zmian hormonalnych u mezczyzn chorych na jaskre prosta otwartego kata przesaczania.
AUTHOR: Nowak M; Swietochowska E; Jochan K; Buntner B
CORPORATE SOURCE: Zakladu Patofizjologii i Endokrynologii Slaskiej AM w Zabrzu.
SOURCE: KLINIKA OCZNA, (2000) 102 (2) 103-8.
Journal code: KWC. ISSN: 0023-2157.
PUB. COUNTRY: Poland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Polish
ENTRY MONTH: 200011
ENTRY WEEK: 20001101
AB INTRODUCTION: Primary open angle ***glaucoma*** (POAG) is the most common type of ***glaucoma*** , pathogenesis of which is not completely known. Several clinical studies show that glucocorticoid hormones may be implicated in the pathogenesis of POAG and ocular hypertension. ***Glucocorticoid*** ***receptors*** have been identified in human outflow tissue of the eye. AIMS: The purpose of this study, therefore, was to evaluate the serum concentration of total cortisol (TF), total testosterone (TT), free testosterone (FT), FSH (follitropin), LH (lutropin), ACTH (adrenocorticotropin), SHBG (sex hormone-binding globulin), DHEA-SO4 (dehydroepiandrosterone sulfate) as well as free cortisol (UFF) and 17-OHCS in 24 hours urinary samples in patients treated because of POAG. PATIENTS AND METHODS: Studies were performed in the group of 30 male patients, aged 55 +/- 13 years, treated because of ***glaucoma*** for more than two years. Serum and urinary concentration of hormones were studied using RIA methods (DPC). RESULTS: The serum concentration of TF (652.03 +/- 315.43 nmol/l), UFF (248.75 +/- 99.39 nmol/l) and 17-OHCS (5.47 +/- 2.64 mg/24 h) in urine was increased compared with control group. There was not significant difference in concentration of pituitary-gonadal axis hormones in glaucomatous and control groups of patients. CONCLUSION: The results could point to the fact that changes in the endocrine system are one of the factors involved in the pathogenesis of POAG. We conclude that an elevated level of cortisol, free cortisol and its metabolites is closely related to the POAG.

L6 ANSWER 6 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999390306 EMBASE
TITLE: A cellular assay distinguishes normal and mutant TIGR/myocilin protein.
AUTHOR: Zhou Z.; Vollrath D.
CORPORATE SOURCE: D. Vollrath, Department of Genetics, Stanford University School Medicine, Lane Building, 300 Pasteur Drive, Stanford, CA 94305-5120, United States. vollrath@genome.stanford.edu
SOURCE: Human Molecular Genetics, (1999) 8/12 (2221-2228).
Refs: 49
ISSN: 0964-6906 CODEN: HMGEE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB ***Glaucoma*** is a blinding eye disease that affects .apprx. 70,000,000 people world-wide. Mutations in the gene TIGR/MYOC have been shown to cause the most common form of the disease, primary open angle ***glaucoma*** , in selected families. Amino acid sequence variants of the gene have been found in 2-4% of sporadic primary open angle ***glaucoma*** cases. Most variants are rare and it is often difficult to definitively distinguish between a deleterious mutation and a benign variant solely on the basis of relative frequencies in patient and control groups. The function of the TIGR/myocilin protein is unknown and an assay to functionally classify variants is lacking. We sought to develop a biochemical assay to distinguish different forms of TIGR/myocilin. We investigated the Triton X-100 detergent solubility characteristics of mutant and normal forms of the protein, expressed by transfection in cultured cells. We observed a clear difference in the behavior of the two types of TIGR/myocilin, all confirmed mutant proteins tested were substantially Triton insoluble, while normal protein and controls were completely soluble. We also tested seven ambiguous variant proteins and classified them as mutant or normal on the basis of their Triton solubility. The results in some cases validated, and in other cases contradicted, earlier classifications of these variants. To our knowledge, Triton solubility is the first example of a general

difference in the
properties of mutant and normal forms of TIGR/myocilin. The assay we have
developed will be useful for discerning protein functional information
from the location of mutations, will aid genetic counseling of individuals
with TIGR/myocilin variants and may provide a clue to understanding a
mechanism by which mutations in TIGR/MYOC cause ***glaucoma***

L6 ANSWER 7 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:274116 BIOSIS
DOCUMENT NUMBER: PREV199900274116
TITLE: Glucocorticoid target receptors and isozymes of
11B-hydroxysteroid dehydrogenase in normal and glaucomatous
human eyes.
AUTHOR(S): Stokes, J. D.; Andrew, R. (1); Seckl, J. R. (1); O'Brien, C.
CORPORATE SOURCE: (1) Dept. of Medicine, Western General Hospital, University
of Edinburgh, Edinburgh UK
SOURCE: IOVS, (March 15, 1999) Vol. 40, No. 4, pp. S669.
Meeting Info.: Annual Meeting of the Association for
Research in Vision and Ophthalmology Fort Lauderdale,
Florida, USA May 9-14, 1999 Association for Research in
Vision and Opthalmology

DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 8 OF 40 MEDLINE
DUPLICATE 1
ACCESSION NUMBER: 1999364864 MEDLINE
DOCUMENT NUMBER: 99364864
TITLE: Effects of glucocorticoids on the trabecular meshwork:
towards a better understanding of ***glaucoma***.
AUTHOR: Wordinger R J; Clark A F
CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of North
Texas, Health Science Center, Fort Worth 76107, USA.
rwording@hsc.unt.edu
SOURCE: PROGRESS IN RETINAL AND EYE RESEARCH, (1999 Sep) 18 (5)
629-67. Ref: 224
Journal code: C2P. ISSN: 1350-9462.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY WEEK: 19991102
AB Glucocorticoid effects on the human trabecular meshwork can be used as a
model system in which to study glaucomatous damage to the trabecular
meshwork. One of the most important risk factors for ***glaucoma*** is
an elevated intraocular pressure. The administration of glucocorticoids
also can cause elevated intraocular pressure in some individuals. In
addition, there is suggestive evidence linking glucocorticoids with the
development of ***glaucoma***. Glucocorticoids cause multiple effects
on the human trabecular meshwork including changes in extracellular matrix
metabolism, organisation of the cytoskeleton, and changes in gene
expression and cell function. New discoveries on the molecular mechanisms
of ***glucocorticoid*** ***receptor*** action provide new
opportunities to study the possible role of this receptor in the
development of ***glaucoma***. For example, alternate spliced forms of
the ***glucocorticoid*** ***receptor***, ***glucocorticoid***
receptor response element half-sites, numerous modulatory factors,
and direct effects of nuclear transcription factors have been recently
described. Other recent information has shown that the new
glaucoma gene (GLC1A/myocilin) is induced in the human trabecular
meshwork by glucocorticoids. Although the exact function of myocilin is
currently unknown, it offers the opportunity to dissect the molecular
pathways regulating aqueous humor outflow. Future challenges include
determining (1) which glucocorticoid effects in the human trabecular
meshwork are responsible for elevated intraocular pressure; and (2) the
significance of these findings to the development of ***glaucoma***.

L6 ANSWER 9 OF 40 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 2000016770 MEDLINE
DOCUMENT NUMBER: 20016770
TITLE: [Mechanism of action of glucocorticoids in asthma].
Les mecanismes d'action moleculaire des glucocorticoides
dans l'asthme.
AUTHOR: Jaffuel D; Mathieu M; Godard P; Michel F B; Demoly P
CORPORATE SOURCE: Service des Maladies Respiratoires, INSERM U454, Hopital
Arnaud-de-Villeneuve, CHU de Montpellier.
SOURCE: REVUE DES MALADIES RESPIRATOIRES, (1999 Sep) 16 (4) 431-42.
Ref: 122
Journal code: RZ9. ISSN: 0761-8425.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY WEEK: 20000204
AB While on the basis of clinical studies glucocorticoids (GC) became the
first-line therapy for asthma, the molecular basis of GC action has been
extensively studied. Glucocorticoids exert their effects by binding to the
glucocorticoid ***receptor*** (GR), which then inhibits or
increases gene transcription through processes known as transrepression
and transactivation, respectively. Transrepression results from the
inhibitory interaction between the GR and other transcription factors like
AP-1 and NF-kappa B. Since AP-1 and NF-kappa B DNA binding sites have been
mapped to the promoter regions of many genes coding for proinflammatory
mediators (IL-1, 2, 5, 6, 8, 13, TNF-alpha, RANTES, Eotaxin, GM-CSF,
metalloproteinases, ICAM-1 ...), this interaction may be an important
aspect of the GC anti-inflammatory properties. Transactivation is mediated
through binding of the GC-activated GR to a DNA sequence called
glucocorticoid response element (GRE) and may result in some benefits and
side effects since GRE has been mapped to the promoter regions of genes
coding for lipocortin, beta 2-adrenergic receptor, and for genes involved
in the onset of metabolic effects (diabetes, hypokaliemia, hydrosodic
retention) and ***glaucoma***. Other molecular mechanisms may also be
involved like the binding to the GR to a negative GRE (nGRE), the
interaction with the basal transcriptional machinery, and the post
transcriptional modulation of mRNA stability. In asthma, the relative
importance of each mechanism remains to be studied, but both mechanisms
may probably be involved.

L6 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:537359 CAPLUS
DOCUMENT NUMBER: 132:34173
TITLE: The preliminary study of ***glucocorticoid***
receptor gene in Chinese patients with
glucocorticoid-induced ***glaucoma***
AUTHOR(S): Zhuo, Yehong; Ge, Jian; Guo, Yan; Lin, Mingkai
CORPORATE SOURCE: Zhongshan Ophthalmic Center, Sun Yat-sen University of
Medical Sciences, Canton, 510060, Peop. Rep. China
SOURCE: Eye Sci. (1999), 15(1), 46-50
CODEN: YAXUE3, ISSN: 1000-4432
PUBLISHER: Zhongshan Ophthalmic Center
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To study the ***glucocorticoid*** ***receptor*** (GR) and the
assocd. gene regulation in the pathogenesis of glucocorticoid-induced
glaucoma (GIG) in Chinese patients. The trabecular cells of
normal individuals and patients with GIG were cultured in vitro. By using
polymerase chain reaction (PCR), gene fragments on GR DNA binding sites of
trabecular cells were amplified. The product was detected by gel
electrophoresis. The trabecular cells were cultured successfully in
normal individuals and patients with GIG in vitro. A single PCR product
was obtained in both two groups with the same size of 545 base pairs.
There is not any difference in gene on the GR DNA binding sites between
normal individuals and patients with GIG. The results suggest the
difference might be in mRNA or other functional genes.
REFERENCE COUNT: 9
REFERENCE(S): (1) Alvarad, J; Invest Ophthalmol Vis Sci 1992, V33, P1120
(2) Bloom, E; J Steroid Biochem 1980, V12, P175 CAPLUS
(3) Fancois, J; Ann Ocul 1954, V187, P805
(4) Holler, S; Science 1985, V318, P635
(5) Jian, G; Eye Science 1996, V12, P64
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD DUPLICATE 3
ACCESSION NUMBER: 1998-333347 [29] WPIDS
DOC. NO. CPI: C1998-103395
TITLE: Diagnosing ***glaucoma*** and determining usefulness
of therapeutic agents - by detecting aberrant expression
of beta ***glucocorticoid*** ***receptor***
DERWENT CLASS: B04 D16
INVENTOR(S): CLARK, A F; WORDINGER, R J
PATENT ASSIGNEE(S): (CLAR-I) CLARK A F; (WORD-I) WORDINGER R J
COUNTRY COUNT: 23

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9824932	A1	19980611 (199829)*		EN	5

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP MX US
AU 9852617 A 19980629 (199845)
EP 943014 A1 19990922 (199943) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9824932	A1	WO 1997-US21054	19971114
AU 9852617	A	AU 1998-52617	19971114
EP 943014	A1	EP 1997-947569	19971114
		WO 1997-US21054	19971114

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9852617	A Based on	WO 9824932
EP 943014	A1 Based on	WO 9824932

PRIORITY APPLN. INFO: US 1996-33227 19961205
AN 1998-333347 [29] WPIDS
AB WO 9824932 A UPAB: 19980722
Diagnosing ***glaucoma*** comprises either:
(i) detecting aberrant ***glucocorticoid*** ***receptor***
(GR) beta expression or defects in a GR gene which encodes GR beta ;
(ii) detecting genetic changes in the GR gene leading to altered GR
beta expression, or
(iii) detecting genetic changes outside the GR gene which lead to
altered GR beta expression.
Also claimed is a method for determining whether an agent is useful
for treating ***glaucoma*** by determining whether it interacts with
GR beta or alters the expression of GR beta .
USE - Cultured human trabecular meshwork cell lines derived from
glaucomatous donors express mRNA for both on alternate splice form of the
human ***glucocorticoid*** ***receptor*** (GR beta), as well as
the normal glucocorticiod receptor (GR alpha), whereas normal tm cell
lines only express mRNA for GR alpha . Determining that an individual
abnormally expresses GR beta in their trabecular meshwork or other tissues
can lead to a diagnosis of ***glaucoma*** . Agents that have
therapeutic value for treating ***glaucoma*** can be determined by
using ligand binding assays or GR beta functional assays.
Dwg.0/0

L6 ANSWER 12 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-437038 [37] WPIDS
DOC. NO. CPI: C1998-132799
TITLE: New 16-hydroxy-11-substituted phenyl-4,9-oestradiene
derivatives - having anti-glucocorticoid activity,
prepared by dehydrating new 5 alpha-hydroxy-9-oestrene
precursors.
DERWENT CLASS: B01
INVENTOR(S): GEBHARD, R; GROEN, M B
PATENT ASSIGNEE(S): (ALKU) AKZO NOBEL NV
COUNTRY COUNT: 70
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9831702	A1	19980723 (199837)*		EN	27

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AM AU BB BG BR BY CA CN CZ EE GE HU ID IS JP KG KP KR LK LR LT LV MD MG MN MX NO NZ PL RO RU SG SI SK TR TT UA US UZ VN
ZA 9800084 A 19980930 (199844) 26
AU 9862935 A 19980807 (199901)
NO 9903459 A 19990907 (199947)
CZ 9902534 A3 20000112 (200009)
EP 973792 A1 20000126 (200010) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 9807079 A 20000418 (200032)
CN 1248262 A 20000322 (200032)
US 6072068 A 20000606 (200033)
NZ 336790 A 20000623 (200038)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9831702	A1	WO 1998-EP377	19980113
ZA 9800084	A	ZA 1998-84	19980106
AU 9862935	A	AU 1998-62935	19980113
NO 9903459	A	WO 1998-EP377	19980113
		NO 1999-3459	19990714
CZ 9902534	A3	WO 1998-EP377	19980113
		CZ 1999-2534	19980113
EP 973792	A1	EP 1998-906887	19980113
		WO 1998-EP377	19980113
BR 9807079	A	BR 1998-7079	19980113
		WO 1998-EP377	19980113
CN 1248262	A	CN 1998-802618	19980113
US 6072068	A	WO 1998-EP377	19980113
		US 1999-341603	19990714
NZ 336790	A	NZ 1998-336790	19980113
		WO 1998-EP377	19980113

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9862935	A Based on	WO 9831702
CZ 9902534	A3 Based on	WO 9831702
EP 973792	A1 Based on	WO 9831702
BR 9807079	A Based on	WO 9831702
US 6072068	A Based on	WO 9831702
NZ 336790	A Based on	WO 9831702

PRIORITY APPLN. INFO: EP 1997-200098 19970115
AN 1998-437038 [37] WPIDS
AB WO 9831702 A UPAB: 19991122
11-substituted-phenyl-oestra-4,9-diene compounds of formula (I), and their
salts and solvates, and precursors of formula (II) are new. R1 = 1-6C
alkyl, 3-6C cycloalkyl, 1-6C alkoxy, triflate, pyridyl or phenyl
(optionally substituted by one or more of CN, halogen and 1-4C alkyl), R2
= H, 1-6C alkyl, 1-oxo-(1-6C alkyl) or carboxy-1-oxo-(1-6C alkyl); R3 = H,
halogen or 1-6C alkyl (optionally substituted by one or more of halogen
and 1-6C alkoxy), R4 = H, 1-6C alkyl, 1-oxo-(1-6C alkyl) or
carboxy-1-oxo-(1-6C alkyl), X = (H,OH), = O, or = NOH, R5 = as R4 or a
protected R4 group; P = protected keto.
USE - (I) have highly selective affinity for ***glucocorticoid***
receptors and have potent in vivo anti-glucocorticoid activity.
They are used in the treatment or prophylaxis of glucocorticoid-dependent
diseases (claimed), e.g. Cushing syndrome, diabetes, ***glaucoma*** ,
sleep disturbances, depression, anxiety, atherosclerosis, hypertension,
obesity, osteoporosis, addiction, withdrawal symptoms, Alzheimer's
disease, schizophrenia, mania, hyperactivity, substance abuse and emesis.
(II) are intermediates for (I).
Dwg.0/0

L6 ANSWER 13 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:243274 BIOSIS
DOCUMENT NUMBER: PREV199800243274
TITLE: A characterization of ***glucocorticoid***
receptor on lymphocytes in patients with
glucocorticoid-induced ***glaucoma*** (GIG.
AUTHOR(S): Ge, J.; Zhou, Y.; Lin, M.; Guo, Y.
CORPORATE SOURCE: Zhongshan Ophthalmic Cent., Sun Yat-sen Univ. Med. Sci., Guanzhou 510060 China
SOURCE: IOVS, (March 15, 1998) Vol. 39, No. 4, pp. S931.
Meeting Info.: Annual Meeting of the Association for
Research in Vision and Ophthalmology Fort Lauderdale,
Florida, USA May 10-15, 1998 Association for Research in
Vision and Ophthalmology
.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 14 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998095893 EMBASE
TITLE: Novel mutations in the TIGR gene in early and late onset
open angle ***glaucoma***
AUTHOR: Mansergh F.C.; Kenna P.F.; Ayuso C.; Kiang A.-S.; Humphries P.; Farrar G.J.
CORPORATE SOURCE: F.C. Mansergh, Wellcome Ocular Genetics Unit, Dept. of
Genetics, Trinity College, Dublin 2, Ireland.
fmnsergh@biotech.bio.tcd.ie
SOURCE: Human Mutation, (1998) 11/3 (244-251).
Refs: 16
ISSN: 1059-7794 CODEN: HUMUE3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A gene for juvenile onset, open angle ***glaucoma*** (JOAG) has been
localized to chromosome 1q21-31 m several families. Mutations in the
trabecular meshwork-induced glucocorticoid response protein (TIGR) gene,
which maps to this region, recently have been found in families
segregating both JOAG and a later onset form of primary open angle
glaucoma (POAG). We have analysed the TIGR gene in two families;
one Spanish family segregating autosomal dominant JOAG and an Irish family
with a later onset form of autosomal dominant POAG. We have found a G-T
transversion in the first base of codon 426 in all affected members of the

Spanish family, which results in a valine to phenylalanine amino acid
substitution. We have also found a G-A transition at the first base of
codon 367 that segregates through all but one branch of the Irish family
and results in a glycine to arginine amino acid substitution. Members of
this family that carry the Gly367Arg change also share a common haplotype
that is neither present in any of the unaffected members of the family,
nor in the branch that does not segregate the mutation. Identification of
further mutations in the TIGR gene increases its importance in the
etiology of open angle ***glaucoma*** .

L6 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:52236 CAPLUS
DOCUMENT NUMBER: 130:247174
TITLE: Characterization of ***glucocorticoid*** ***receptor*** on lymphocytes in Chinese patients with glucocorticoid-induced ***glaucoma***
AUTHOR(S): Zhuo, Yehong; Ge, Jian; Guo, Yan
CORPORATE SOURCE: Zhongshan Ophthalmic Center, Sun Yat-sen University of Medical Sciences, Canton, 510060, Peop. Rep. China
SOURCE: Eye Sci. (1998), 14(3), 145-148
CODEN: YAXUE3; ISSN: 1000-4432
PUBLISHER: Zhongshan Ophthalmic Center
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors studied the pathogenesis of glucocorticoid-induced ***glaucoma*** (GIG) through characterization of ***glucocorticoid*** ***receptor*** (GR) on lymphocytes in Chinese patients with GIG. By radioligand receptor binding followed by Scatchard anal., the specific binding sites were characterized and quantitated for ***glucocorticoid*** ***receptors*** on peripheral blood lymphocytes obtained from patients with GIG and the control group. The binding sites the authors detected were as follows: 12.7.+-.1.47.times.103 receptors per cell with a KD of 3.02.+-.0.62nmol/L in patients with GIG, 7.26.+-.0.45.times.103 receptors per cell with a KD of 3.03.+-.0.56nmol/L in the control group. The statistical difference of receptors per cell is significant between two groups, patients with GIG having more GR binding sites, while the difference of Kd is not significant. The preliminary findings suggest that patients with GIG are more sensitive to glucocorticoid and the increase of binding sites of GR may be the receptor and mol. basis of the pathogenesis of GIG.
REFERENCE COUNT: 17
REFERENCE(S): (6) Benezra, D; Am J Ophthalmol 1976, V82, P806 CAPLUS
(8) Bloom, E; J Steroid Biochem 1980, V12, P175 CAPLUS
(11) Evans, R; Science 1988, V240, P889 CAPLUS
(12) Foon, K; Am J Ophthalmol 1977, V83, P167 CAPLUS
(15) Howard, K; J Biol Chem 1990, V265, P11928 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998135472 EMBASE
TITLE: Juvenile open angle ***glaucoma***: Fine mapping of the TIGR gene to 1q24.3-q25.2 and mutation analysis
AUTHOR: Michels-Rautenstrauss K.G.; Mardin C.Y.; Budde W.M.; Liehr T.; Polansky J.; Nguyen T., Timmerman V., Van Broeckhoven C.; Naumann G.O.H.; Pfeiffer R.A.; Rautenstrauss B.W.
CORPORATE SOURCE: B.W. Rautenstrauss, Institute of Human Genetics, FAU of Erlangen-Nurnberg, Schwabachanlage 10, D-91054 Erlangen, Germany. BERNDWR@HUMGENET.UNI-ERLANGEN.DE
SOURCE: Human Genetics, (1998) 102/1 (103-106).
Refs: 15
ISSN: 0340-6717 CODEN: HUGEDQ
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Autosomal dominant juvenile open angle ***glaucoma*** (JOAG) is an early-onset form of primary open angle ***glaucoma*** (POAG), which has been linked to chromosome 1q21-q31. Recently, mutations in the trabecular meshwork inducible glucocorticoid response gene (TIGR), one of the candidate genes mapped in this region, were identified in ***glaucoma*** patients of several families. We screened for mutations of the TIGR gene in two German families with JOAG and in 100 unselected sporadic cases of POAG. In the first family we identified a Pro370Leu mutation and in the second family a Gly367Arg mutation cosegregating with the ***glaucoma*** phenotype. No pathogenic mutation was found in 100 sporadic cases but a Tyr347Tyr polymorphism was found in two patients. Furthermore, fluorescence in situ hybridization (FISH) analysis was used to map a TIGR-specific yeast artificial chromosome to 1q24.3-q25.2.

L6 ANSWER 17 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:187654 BIOSIS
DOCUMENT NUMBER: PREV199800187654
TITLE: Supplement: Efficacy and safety of inhaled corticosteroids: New developments.
AUTHOR(S): Barnes, Peter J. (1); Pedersen, Soren; Busse, William W.
CORPORATE SOURCE: (1) Dep. Thoracic Med., National Heart Lung Inst., Imperial College, Dovehouse St., London SW3 6LY UK
SOURCE: American Journal of Respiratory and Critical Care Medicine, (March, 1998) Vol. 157, No. 3 PART 2, pp. S1-S53. ISSN: 1073-449X.
DOCUMENT TYPE: General Review
LANGUAGE: English

L6 ANSWER 18 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1997-193257 [18] WPIDS
DOC. NO. CPI: C1997-061851
TITLE: New 11-(substd. phenyl) oestra-4,9-diene derivs. - having anti-glucocorticoid activity used to treat e.g. Cushing syndrome, diabetes, ***glaucoma*** , sleep disturbances, depression or atherosclerosis.
DERWENT CLASS: B01
INVENTOR(S): GEBHARD, R
PATENT ASSIGNEE(S): (ALKU) AKZO NOBEL NV
COUNTRY COUNT: 32
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
AU 9662119	A	19970220 (199718)*			22
EP 763541	A1	19970319 (199718)		EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
NO 9603427	A	19970218 (199719)			
ZA 9606555	A	19970430 (199723)			19
CA 2182771	A	19970218 (199725)			
CZ 9602386	A3	19970514 (199726)			
JP 09104696	A	19970422 (199726)			9
NZ 299181	A	19970922 (199745)			
HU 9602269	A2	19970428 (199801)			
KR 97010784	A	19970327 (199814)			
MX 9603476	A1	19970701 (199827)			
BR 9603429	A	19980512 (199828)			
SG 52834	A1	19980928 (199904)			
EP 763541	B1	19990728 (199934)		EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 69603425	E	19990902 (199942)			
NO 306257	B1	19991011 (199949)			
AU 711369	B	19991014 (200001)			
ES 2137625	T3	19991216 (200006)			
US 6011025	A	20000104 (200008)			
RU 2135514	C1	19990827 (200033)			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
AU 9662119	A	AU 1996-62119	19960816
EP 763541	A1	EP 1996-202273	19960813
NO 9603427	A	NO 1996-3427	19960816
ZA 9606555	A	ZA 1996-6555	19960801
CA 2182771	A	CA 1996-2182771	19960806
CZ 9602386	A3	CZ 1996-2386	19960813
JP 09104696	A	JP 1996-212824	19960812
NZ 299181	A	NZ 1996-299181	19960815
HU 9602269	A2	HU 1996-2269	19960816
KR 97010784	A	KR 1996-33671	19960814
MX 9603476	A1	MX 1996-3476	19960816
BR 9603429	A	BR 1996-3429	19960814
SG 52834	A1	SG 1996-10458	19960814
EP 763541	B1	EP 1996-202273	19960813
DE 69603425	E	DE 1996-603425	19960813
		EP 1996-202273	19960813
NO 306257	B1	NO 1996-3427	19960816
AU 711369	B	AU 1996-62119	19960816
ES 2137625	T3	EP 1996-202273	19960813
US 6011025	A Cont of	US 1996-696081	19960813
		US 1997-935360	19970922
RU 2135514	C1	RU 1996-115774	19960816

FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 69603425	E Based on	EP 763541
NO 306257	B1 Previous Publ.	NO 9603427
AU 711369	B Previous Publ.	AU 9662119
ES 2137625	T3 Based on	EP 763541

PRIORITY APPLN. INFO: EP 1995-202229 19950817
AN 1997-193257 [18] WPIDS
AB AU 9662119 A UPAB: 19970502
11-(substd. phenyl) oestra-4,9-diene derivs. of formula (I) are new. A = a
residue of a 5 or 6-membered ring contg. 2 heteroatoms which are not
connected to each other and are selected form O or S, and the ring is opt.
substd. by one or more halo atoms; or the residue of a 5 or 6-membered
ring where no C=C double bonds are present and the ring contains one
heteroatom O or S and the heteroatom is connected to the phenyl gp. at
the position marked with the asterisk, and the ring is opt. substd. by one
or more halo atoms; R1 = H or 1-oxo(1-4C alkyl), R2 = H, 1-8C alkyl, halo
or CF3, X = (H,OH), O or NOH; the dotted line represents a double or
triple bond.
USE - (I) show high ***glucocorticoid*** ***receptor*** binding affinity and have high in vivo anti-glucocorticoid activity. They
can be used in the treatment and/or prophylaxis of glucocorticoid-
dependent diseases e.g. Cushing syndrome, diabetes, ***glaucoma*** ,
sleep disturbances, depression, anxiety, atherosclerosis, hypertension,
adiposity, osteoporosis and withdrawal symptoms from narcotics and their
mixts.
ADVANTAGE - (I) lack appreciable affinity for mineralocorticoid,
progesterone, oestrogen and androgen receptors, indicating a clean
side-effect profile.
Dwg.0/0

L6 ANSWER 19 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97344241 EMBASE
DOCUMENT NUMBER: 1997344241
TITLE: Recurrent mutations in a single exon encoding the
evolutionarily conserved olfactomedin-homology domain of
TIGR in familial open-angle ***glaucoma*** .
AUTHOR: Adam M.F.; Belmouden A.; Binisti P.; Brezin A.P.; Valtot
F.; Bechetoille A.; Dascotte J.-C.; Copin B.; Gomez L.;
Chaventre A.; Bach J.-F.; Garchon H.-J.
CORPORATE SOURCE: H.-J. Garchon, INSERM U25, Hopital Necker, 161 rue de
Sevres, 75743 Paris cedex 15, France.
garchon@necker.fr
SOURCE: Human Molecular Genetics, (1997) 6/12 (2091-2097).
Refs: 23
ISSN: 0964-6906 CODEN: HMGEE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Primary open-angle ***glaucoma*** (POAG) is a highly prevalent cause
of irreversible blindness which associates cupping of the optic disc and
alteration of the visual field, elevation of intraocular pressure being a
major risk factor. Provided diagnosis is made at an early stage,
treatments are available to prevent visual impairment. A locus, GLC1A, has
been mapped on chromosome 1q23-q25 in several families affected with
juvenile-onset POAG (JOAG) and also in some families affected with
juvenile and middle-age onset POAG. Recently, three mutations of the TIGR
(Trabecular meshwork-Induced Glucocorticoid Response) gene were shown to
be responsible for the disease in several American families and in
unrelated POAG patients. We now describe five new mutations in eight
French families. All mutations known to date appear to concentrate in the
evolutionarily conserved C-terminal domain of TIGR which bears homology to
frog olfactomedin, an extracellular matrix glycoprotein of the olfactory
epithelium, to rat and human neuronal olfactomedin-related proteins and to
F11C3.2, a protein from Caenorhabditis elegans. Moreover, this conserved
domain of TIGR is encoded by a single exon to which mutation screening
could be limited. Surprisingly, the TIGR message, which is abundantly
transcribed in the trabecular meshwork and also in the ciliary body and
the sclera, is not expressed in the optic nerve whose degeneration is,
however, the primary lesion of POAG.

L6 ANSWER 20 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97288657 EMBASE
DOCUMENT NUMBER: 1997288657
TITLE: Recent advances in molecular genetics of ***glaucomas***
AUTHOR: Sarfarazi M.
CORPORATE SOURCE: M. Sarfarazi, Surgical Research Center, Department of
Surgery, Univ. Connecticut Health Center, Farmington, CT
06030-1110, United States.
msarfara@cortex.uchc.edu
SOURCE: Human Molecular Genetics, (1997) 6/10 REV. ISS.
(1667-1677).
Refs: 93
ISSN: 0964-6906 CODEN: HMGEE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB ***Glaucomas*** are a heterogeneous group of eye conditions with
manifestation from as early as birth to very late age of onset in life.
The primary type of these conditions affecting children and juveniles are
less frequent, but the prevalence of ***glaucomas*** affecting older
people of .ltoreq. 70 years progressively rises to .apprx. 5%. The
molecular genetics of three types of ***glaucoma*** have been the
subject of investigation in the last few years. As a result, two loci
(GLC3A and GLC3B) have been identified for primary congenital
glaucoma , one locus (GLC1A) for juvenile-onset primary open angle
glaucoma and a further two loci (GLC1B and GLC1C) for late-onset
chronic open angle ***glaucoma*** . Early this year, the first set of
mutations was described in the CYP1B1 (Cytochrome P4501B1) and TIGR
(Trabecular meshwork Inducible Glucocorticoid Response Protein) genes for
the GLC3A and GLC1A-linked families, respectively. The mapping of
different types of ***glaucoma*** and mutation identification in these
two genes are the focus of this review

L6 ANSWER 21 OF 40 MEDLINE
DUPLICATE 4
ACCESSION NUMBER: 97315957 MEDLINE
DOCUMENT NUMBER: 97315957
TITLE: PCR-SSCP analysis of the glucocorticoid-responsive element
of the atrial natriuretic peptide gene in familial primary
open-angle ***glaucoma*** .
AUTHOR: Richardson K.A.; Tunny T.J.; Clark C.V.
CORPORATE SOURCE: University Department of Medicine, Greenslopes Private
Hospital, Brisbane, Queensland, Australia.
SOURCE: CLINICAL AND EXPERIMENTAL PHARMACOLOGY AND PHYSIOLOGY,
(1997 Jun) 24 (6) 427-9.
Journal code: DD8. ISSN: 0305-1870.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY WEEK: 19970904
AB 1. Familial primary open-angle ***glaucoma*** (POAG) is a
heterogeneous disease of unknown aetiology and the elucidation of the
underlying genetic mechanisms contributing to phenotypic expression will
be essential if earlier diagnosis of at-risk individuals and more specific
medical treatment can be achieved. In a significant percentage of patients
with POAG, intraocular pressure increases in response to topical ocular
glucocorticoids. 2. Atrial natriuretic peptide (ANP) assists in the
regulation of intraocular pressure levels and binding of the
glucocorticoid ***receptor*** dimer to the
glucocorticoid-responsive element in intron 2 of the ANP gene has been
shown to increase ANP mRNA levels in vitro. We amplified and examined this
sequence in the ANP gene by PCR-SSCP analysis in 100 patients with
familial POAG and in 60 normal control subjects. No base alterations in
the amplified product were found. 3. Thus, the present study found no
evidence for an alteration in the sequence of the glucocorticoid-
responsive element of the ANP gene that could alter ANP gene transcription
in patients with familial POAG. The mechanism responsible for the increase
in intraocular pressure levels in response to glucocorticoids is most
likely independent of the glucocorticoid-responsive element in the ANP
gene.

L6 ANSWER 22 OF 40 SCISEARCH COPYRIGHT 2000 ISI (R)
ACCESSION NUMBER: 96:286937 SCISEARCH
THE GENUINE ARTICLE: UD853
TITLE: INHIBITION OF DEXAMETHASONE-INDUCED CYTOSKELETAL CHANGES
IN CULTURED HUMAN TRABECULAR MESHWORK CELLS BY
TETRAHYDROCORTISOL
AUTHOR: CLARK A F (Reprint), LANE D; WILSON K; MIGGANS S T;
MCCARTNEY M D
CORPORATE SOURCE: ALCON LABS INC, GLAUCOMA RES R241, 6201 S FREEWAY, FT WORTH, TX, 76134 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, (APR 1996)
Vol. 37, No. 5, pp. 805-813.
ISSN: 0146-0404.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 47
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Purpose, To determine the cellular mechanism of action of the
intraocular pressure (IOP) lowering steroid tetrahydrocortisol (THF).
Methods, Tetrahydrocortisol was evaluated for glucocorticoid antagonist
activity using in vitro and in vivo assays. Systemically administered THF
was evaluated for its ability to inhibit dexamethasone-induced body weight
loss and systemic hypertension in rats. In vitro receptor antagonism was
tested using the supernatant fraction of IM9 cells as the source of
soluble ***glucocorticoid*** ***receptor*** in H-3-dexamethasone
displacement binding assays. In addition, six different primary human
trabecular meshwork (TM) cell lines were cultured for 0 to 14 days in the
absence or presence of dexamethasone (10(-7) M) and/or THF (10(-6) to
10(-6) M). The effects of these steroids on the TM cytoskeleton were
determined by epifluorescent microscopy and by transmission electron
microscopy.
Results, Tetrahydrocortisol was unable to inhibit the dexamethasone
(DEX)-induced systemic hypertension and decrease in body mass in rats and
was unable to displace H-3-DEX from the soluble human
glucocorticoid ***receptor*** . However, THF inhibited the
DEX-induced formation of cross-linked actin networks in cultured human TM
cells in a progressive and dose-dependent manner (IC50 = 5.7 x 10(-7) M).
Dexamethasone caused changes in the TM cell microtubules that were
reversed partially by concomitant treatment with THF. Tetrahydrocortisol
alone appeared to increase microfilament bundling in TM cells.
Conclusions. Tetrahydrocortisol was not a glucocorticoid antagonist at
the level of the classical ***glucocorticoid*** ***receptor*** and
did not appear to antagonize systemically mediated glucocorticoid activity
in the rat, Tetrahydrocortisol inhibited DEX-induced changes in the TM
microfilaments and microtubules. These results may explain partially the
IOP lowering activity of THF because glucocorticoid-mediated changes in
the TM cytoskeleton have been proposed to be involved in the generation of
ocular hypertension.

L6 ANSWER 23 OF 40 MEDLINE
DUPLICATE 5
ACCESSION NUMBER: 96330663 MEDLINE
DOCUMENT NUMBER: 96330663
TITLE: Fluticasone propionate: topical or systemic effects?.
AUTHOR: Howland W C 3rd
CORPORATE SOURCE: Healthquest Research, Austin, Texas 78759, USA.
SOURCE: CLINICAL AND EXPERIMENTAL ALLERGY, (1996 May) 26 Suppl 3
18-22.
Journal code: CEB. ISSN: 0954-7894.
PUB COUNTRY: ENGLAND: United Kingdom
(CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY WEEK: 19970304
AB Intranasal corticosteroids have been shown to be more effective than oral
antihistamines for the treatment of seasonal allergic rhinitis. However,
there are some who question whether intranasally administered
corticosteroids should be used due to potential systemic effects.
Fluticasone propionate, a potent corticosteroid with high specificity for
the ***glucocorticoid*** ***receptor*** , is available as an
aqueous nasal spray for the treatment of allergic rhinitis. To determine
whether the efficacy of fluticasone propionate aqueous nasal spray (FPANS)
was due to direct topical effects on the nasal mucosa or to indirect
systemic effects following absorption from the nasal mucosa or from the
swallowed portion of an intranasal dose, FPANS 200 micrograms once daily
was compared with oral fluticasone propionate 5 mg or 10 mg once daily or
placebo for 2 weeks in patients with seasonal allergic rhinitis. These
oral dosages were chosen to yield low but consistent plasma fluticasone
propionate concentrations. Both clinician- and patient-rated scores for
nasal obstruction, rhinorrhoea, sneezing, and nasal itching were
significantly lower in the intranasal fluticasone propionate group
compared with both oral fluticasone propionate groups. A separate
placebo-controlled study was conducted in patients with perennial rhinitis
to determine if administration of FPANS 200 micrograms once daily for 1
year was associated with adverse systemic effects. At the 1-year
assessment, there were no significant effects on bone mineral density or
on biochemical markers of bone turnover. Similarly, there was no evidence
of posterior subcapsular cataracts nor of ***glaucoma*** . Furthermore,
there were no significant effects on hypothalamic-pituitary adrenal axis
function as assessed by plasma cortisol and 24-h urinary cortisol response
to the 6-h cosyntropin stimulation test. These data confirm that the
efficacy of FPANS for the treatment of allergic rhinitis results from
direct topical effects, thus reducing the likelihood of adverse systemic
effects.

L6 ANSWER 24 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96153145 EMBASE
DOCUMENT NUMBER: 1996153145
TITLE: Fluticasone propionate: Topical or systemic effects?.
AUTHOR: Howland III W.C.
CORPORATE SOURCE: Healthquest Research, 3807 Spicewood Springs Road,Austin,
TX 78759, United States
SOURCE: Clinical and Experimental Allergy, Supplement, (1996) 26/3
(18-22).
ISSN: 0960-2178 CODEN: CLASEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
011 Otorhinolaryngology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Intranasal corticosteroids have been shown to be more effective than oral
antihistamines for the treatment of seasonal allergic rhinitis. However,
there are some who question whether intranasally administered
corticosteroids should be used due to potential systemic effects.
Fluticasone propionate, a potent corticosteroid with high specificity for
the ***glucocorticoid*** ***receptor*** , is available as an
aqueous nasal spray for the treatment of allergic rhinitis. To determine
whether the efficacy of fluticasone propionate aqueous nasal spray (FPANS)
was due to direct topical effects on the nasal mucosa or to indirect
systemic effects following absorption from the nasal mucosa or from the
swallowed portion of an intranasal dose, FPANS 200 .mu g once daily was
compared with oral fluticasone propionate 5 mg or 10 mg once daily or
placebo for 2 weeks in patients with seasonal allergic rhinitis. These
oral dosages were chosen to yield low but consistent plasma fluticasone
propionate concentrations. Both clinician- and patient-rated scores for
nasal obstruction, rhinorrhoea, sneezing, and nasal itching were
significantly lower in the intranasal fluticasone propionate group
compared with both oral fluticasone propionate groups. A separate
placebo-controlled study was conducted in patients with perennial rhinitis
to determine if administration of FPANS 200 .mu.g once daily for 1 year
was associated with adverse systemic effects. At the 1-year assessment,
there were no significant effects on bone mineral density or on
biochemical markers of bone turnover. Similarly, there was no evidence of
posterior subcapsular cataracts nor of ***glaucoma*** . Furthermore,
there were no significant effects on hypothalamic-pituitary adrenal axis
function as assessed by plasma cortisol and 24-h urinary cortisol response
to the 6-h cosyntropin stimulation test. These data confirm that the
efficacy of FPANS for the treatment of allergic rhinitis results from
direct topical effects, thus reducing the likelihood of adverse systemic
effects.

L6 ANSWER 25 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95173327 EMBASE
DOCUMENT NUMBER: 1995173327
TITLE: Ophthalmic corticosteroids and steroid ***glaucoma***
mechanisms.
AUTHOR: Polansky J.R.; Fauss D.J.; Nguyen T.D.
CORPORATE SOURCE: Department of Ophthalmology, UCSF School of Medicine,San
Francisco, CA 94143-0730, United States
SOURCE: Ophthalmology Clinics of North America, (1995) 8/2
(215-228+ix).
ISSN: 0896-1549 CODEN: OCNAF2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Studies of basic pharmacologic parameters, including
glucocorticoid ***receptor*** -binding, susceptibility to
metabolism, and active drug levels in the aqueous humor by radio-receptor
assay have helped to define potentially important differences in the
ophthalmic corticosteroids available for clinical use. Information gained
by these evaluations has aided in the interpretation of prior in vivo
clinical and experimental animal data with regards to

both
anti-inflammatory effects and the propensity of these drugs to raise
intraocular pressure (IOP). Potentially relevant new leads to evaluate the
IOP side-effects of corticosteroids have also been developed by evaluating
dexamethasone regulation of specific protein synthesis and cell division
in human trabecular meshwork endothelial cells, as the probable 'target
cell' for the observed reduction in outflow facility.

L6 ANSWER 26 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1995:272333 BIOSIS
DOCUMENT NUMBER: PREV199598286633
TITLE: Clinical uses of antiprogestogens.
AUTHOR(S): Van Look, Paul F. A. (1); Von Hertzen, Helena
CORPORATE SOURCE: (1) Special Programme Res., Dev. Res. Training Human
Reproduction, World Health Organization, Avenue Appia, 1211
Geneva 27 Switzerland
SOURCE: Human Reproduction Update, (1995) Vol. 1, No. 1, pp. 19-34.
ISSN: 1355-4786.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB Antiprogestogens, which block the action of progesterone at the cellular
level through binding to the progesterone receptor, are proving to be one
of the most significant developments in endocrinology in recent years.
Several hundreds of such compounds have been synthesized, but only a few
of them have been evaluated to any significant extent in biological
screening models and, to our knowledge, only three compounds, namely
mifepristone, lilopristone (ZK 98.734) and onapristone (ZK 98.299) have
been given to humans. Most of the clinical research to date has focused on
the use of mifepristone given in combination with prostaglandin for
termination of early pregnancy, an indication for which the compound is
being used routinely in four countries so far, i.e. China, France, the UK
and Sweden. The gynaecological and obstetrical applications in which
antiprogestogens have been shown to be of value to date include ripening
of the pregnant cervix prior to pregnancy termination, sensitization of
the uterus to prostaglandins in second-trimester abortion, and induction
of labour. Available data suggest that antiprogestogens have no place in
the conservative treatment of ectopic pregnancy or in the treatment of
premenstrual tension. In fertility regulation, the sequential combination
regimen of mifepristone plus prostaglandin as used for inducing abortion
has proved to be effective also for menses induction and can be expected
to be an efficacious once-a-month contraceptive. Mifepristone alone,
without adjuvant prostaglandin, has yielded promising results as an
anti-implantation agent and in emergency contraception. Other potential
uses include once-a-week contraception, ovulation inhibition (in a
sequential regimen with a progestogen), and as a daily mini-pill.
Mifepristone, and other antiprogestogens for which biological data have
been reported also bind to the cellular receptors for glucocorticoid
hormones and, consequently, possess antiglucocorticoid in addition to
their antiprogestational activity. Because of this antiglucocorticoid
effect, mifepristone has been employed successfully in the palliative
treatment of hypercortisolism due to Cushing's syndrome, and its use has
been proposed for treating certain forms of depression and of
glaucoma , and in wound healing. However, for scientific and
practical reasons, it would be preferable if molecules were developed that
have only the antiprogestational or the antiglucocorticoid activity rather
than both.

L6 ANSWER 27 OF 40 MEDLINE
DUPLICATE 6
ACCESSION NUMBER: 94131755 MEDLINE
DOCUMENT NUMBER: 94131755
TITLE: Glucocorticoid-induced formation of cross-linked actin
networks in cultured human trabecular meshwork cells.
AUTHOR: Clark A F; Wilson K; McCartney M D; Miggans S T; Kunkle M;
Howe W
CORPORATE SOURCE: Alcon Laboratories, Inc., Fort Worth, Texas 76134.
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1994 Jan)
35 (1) 281-94.
Journal code: GWI. ISSN: 0146-0404.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
AB PURPOSE. To determine the effects of glucocorticoid treatment on the
microfilament structure of cultured human trabecular meshwork cells.
Topical or systemic administration of glucocorticoids can lead to the
development of ocular hypertension and to the development of vision loss,
which is clinically similar to primary open angle ***glaucoma*** .
However, the mechanism(s) by which glucocorticoids cause ocular
hypertension is not well defined. Alterations in the trabecular meshwork,
the site of drainage of aqueous humor from the eye, have been linked to
the development of ocular hypertension. METHODS. Human trabecular meshwork
cells were cultured in the presence and absence of glucocorticoids for 0
to 21 days. The microfilament organization of the cultured trabecular
meshwork cells was examined by epifluorescent and transmission electron
microscopy. RESULTS. Glucocorticoids caused a progressive change in the
organization of microfilaments in the trabecular meshwork cells, but not
in other cultured ocular cells. By fluorescence microscopic analysis, the
actin stress fibers found in control trabecular meshwork cells were
reorganized on treatment with glucocorticoids into cross-linked actin
networks that resembled geodesic-dome-like polygonal lattices. The
cross-linked actin networks were reversible on withdrawal of the
glucocorticoid treatment. Dose-response data for dexamethasone, relative
ranking of activity with glucocorticoid potency, and partial inhibition
with glucocorticoid antagonists all suggest the involvement of the
trabecular meshwork ***glucocorticoid*** ***receptor*** in
cross-linked actin network formation. The reorganization of the trabecular
meshwork cytoskeleton alters cell function because glucocorticoid
treatment of cultured trabecular meshwork cells also inhibited trabecular
meshwork cell migration and proliferation. CONCLUSION. The steroid-induced
alteration in trabecular meshwork cytoskeleton may be an important factor
in the development of steroid-induced ocular hypertension and may play a
role in the ocular hypertension associated with primary open angle
glaucoma .

L6 ANSWER 28 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1992:330593 BIOSIS
DOCUMENT NUMBER: BA94:32434
TITLE: MIFEPRISTONE BLOCKS SPECIFIC ***GLUCOCORTICOID*** ***RECEPTOR*** BINDING IN RABBIT IRIS-CILIARY BODY.
AUTHOR(S): MUNDEN P M; SCHMIDT T J
CORPORATE SOURCE: DEP. OPHTHALMOL., UNIV. IOWA HOSP. CLIN., IOWA CITY, IOWA 52242
SOURCE: ARCH OPHTHALMOL, (1992) 110 (5), 703-705.
CODEN: AROPAW. ISSN: 0003-9950.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Mifepristone is a specific ***glucocorticoid*** ***receptor***
antagonist that has been shown to lower intraocular pressure modestly when
applied topically to rabbit eyes. We evaluated the ability of mifepristone
to block specific in vitro ***glucocorticoid*** ***receptor***
binding to the labeled agonist triamcinolone acetonide in cytosol isolated
from rabbit iris-ciliary body tissue. A 500-fold molar excess of
nonradioactive mifepristone completely blocked specific binding of
triamcinolone acetonide to ***glucocorticoid*** ***receptors***
in the iris-ciliary body cytosol. Additionally, specific binding was
blocked in a dose-dependent fashion over a range of 0.005-fold to 500-fold
molar excess of mifepristone. Mifepristone's effect on intraocular
pressure may be due to its ability to antagonize ***glucocorticoid***
receptor -mediated effects in ocular tissues.

L6 ANSWER 29 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92350940 EMBASE
DOCUMENT NUMBER: 1992350940
TITLE: Role of receptors in the trabecular meshwork of the eye as
targeted to the development of antiglaucoma therapy.
AUTHOR: Tripathi R.C.; Yang C.; Tripathi B.J.; Borisuth N.S.C.
CORPORATE SOURCE: University of Chicago, Visual Sciences Center, 939 East
57th Street,Chicago, IL 60637, United States
SOURCE: Drug Development Research, (1992) 27/3 (191-228).
ISSN: 0272-4391 CODEN: DDREDK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology
012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The major pathway for the outflow of aqueous humor from the anterior
chamber of the eye is the trabecular meshwork/Schlemm's canal system. The
meshwork is composed of connective tissue beams that are ensheathed by
trabecular cells, these cells derive their nutrition from the aqueous
humor and thus are uniquely susceptible to

morphologic and biochemical
regulation by bioactive substances that are present or released in this
fluid and to pharmacologic agents that are targeted to act on the tissue.
The receptors that have been detected on trabecular cells include those
for growth modulatory peptides (bFGF, TGF- beta.1, transferrin, IGF-1, and
EGF), epinephrine, dopamine, glucocorticoids, benzodiazepines,
prostanoids, biogenic amines, the Fc portion of IgGs, and probably those
for molecules of the extracellular matrix (integrins). Selective up- or
down-regulation of the receptors on the trabecular cells would facilitate
an effective control of the intraocular pressure in diseased conditions of
the eye. We discuss the prospects and hurdles in the utilization of
receptor targeting as a therapeutic modality for trabecular cell
regeneration in ***glaucoma*** as well as for pharmacologic
trabeculectomy and as a treatment for hypotony after ***glaucoma***
filtration surgery. We believe that regulation of receptor expression is a
novel method for the development of new antiglaucoma agents and for
minimizing the side effects of drugs that are administered topically and
systemically for the control of the intraocular pressure.

L6 ANSWER 30 OF 40 MEDLINE
DUPLICATE 7
ACCESSION NUMBER: 91201034 MEDLINE
DOCUMENT NUMBER: 91201034
TITLE: Increased plasma noncortisol glucocorticoid activity in
open-angle ***glaucoma*** [published erratum appears in
Invest Ophthalmol Vis Sci 1991 Jul;32(8):2440].
AUTHOR: McCarty G R, Schwartz B
CORPORATE SOURCE: Department of Ophthalmology, New England Medical Centre
Hospitals, Boston, Massachusetts 02111.
CONTRACT NUMBER: EY00024 (NEI)
EY07045 (NEI)
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1991 Apr)
32 (5) 1600-8
Journal code: GWI. ISSN: 0146-0404.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
AB Total biologic plasma glucocorticoid activity of normal, ocular
hypertensive, and open-angle ***glaucoma*** patients was compared
using a ***glucocorticoid*** ***receptor*** -based competitive
binding assay. Multiple linear-regression analysis was used to adjust for
the effects of significant ocular and nonocular variables, including
therapy for ***glaucoma***. The ***glaucoma*** patients had
significantly greater plasma glucocorticoid activities than did normal
subjects. A comparison of receptor-based assay values to values obtained
with a cortisol radioimmunoassay showed that significant amounts of
biologic glucocorticoid activity in the plasma of the ***glaucoma***
patients could not be explained by cortisol alone. In the normal and
ocular hypertensive groups, however, virtually all of the plasma
glucocorticoid activity could be accounted for by cortisol. These results
suggest that in open-angle ***glaucoma*** patients, noncortisol
glucocorticoids are responsible for elevating biologic plasma
glucocorticoid activity. Thus, open-angle ***glaucoma*** may be
associated with a disturbance of the hypothalamic-pituitary-adrenal axis
that produces increased plasma levels of both cortisol and other
noncortisol glucocorticoids.

L6 ANSWER 31 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1990-022375 [03] WPIDS
DOC. NO. CPI: C1990-009886
TITLE: New 11-aryl-19-nor-progesterone derivs. - useful as
progestational or anti-progestational agents and/or
anti-glucocorticoid agents.
DERWENT CLASS: B01
INVENTOR(S): COOK, C E, LEE, Y, RECTOR, D; REEL, J R; WANI, M C; COOK, E, REEL, J
PATENT ASSIGNEE(S): (RETR-N) RES TRIANGLE INST
COUNTRY COUNT: 18
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8912448	A	19891228	(199003)*	EN	50
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU DK JP KR NO					
AU 8938506	A	19900112	(199013)		
US 4954490	A	19900904	(199038)		
EP 422100	A	19910417	(199116)		
R: AT BE CH DE FR GB IT LI LU NL SE					
NO 9005546	A	19901221	(199116)		
DK 9003053	A	19901221	(199131)		
US 5073548	A	19911217	(199202)		
JP 03505582	W	19911205	(199204)		
AU 635211	B	19930318	(199318)		
EP 422100	A4	19940427	(199530)		
NO 178264	B	19951113	(199550)		
EP 422100	B1	19970312	(199715)	EN	28
R: AT BE CH DE FR GB IT LI LU NL SE					
CA 1338906	C	19970211	(199718)		
DE 68927861	E	19970417	(199721)		
JP 2953725	B2	19990927	(199945)		19
KR 161975	B1	19981116	(200030)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8912448	A	WO 1989-US2706	19890623
US 4954490	A	US 1988-210503	19880623
EP 422100	A	EP 1989-907924	19890623
US 5073548	A	US 1990-504129	19900403
JP 03505582	W	JP 1989-507392	19890623
AU 635211	B	AU 1989-38506	19890623
EP 422100	A4	EP 1989-907924	
NO 178264	B	WO 1989-US2706	19890623
		NO 1990-5546	19901221
EP 422100	B1	EP 1989-907924	
		WO 1989-US2706	19890623
CA 1338906	C	CA 1989-603686	19890622
DE 68927861	E	DE 1989-627861	19890623
		EP 1989-907924	19890623
		WO 1989-US2706	19890623
JP 2953725	B2	JP 1989-507392	19890623
		WO 1989-US2706	19890623
KR 161975	B1	KR 1990-700406	19900222

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 635211	B Previous Publ	AU 8938506
	Based on	WO 8912448
NO 178264	B Previous Publ.	NO 9005546
EP 422100	B1 Based on	WO 8912448
DE 68927861	E Based on	EP 422100
	Based on	WO 8912448
JP 2953725	B2 Previous Publ.	JP 03505582
	Based on	WO 8912448

PRIORITY APPLN. INFO: US 1988-210503 19880623
AN 1990-022375 [03] WPIDS
AB WO 8912448 A UPAB: 19930928
Beta-Aryl-19-norprogesterones of formula (I) are new. Where R1 = H, 1-4C
alkyl, 2-4C alkenyl, 2-4C alkynyl, 0H, 0C0Me or 0C0R5; R5 = 2-8C alkyl,
2-8C alkenyl, 2-8C alkynyl or aryl; R2 = H; R3 = H, 1-4C alkyl, 2-4C
alkenyl or 2-4C alkynyl. R4 = H, Me, F or Cl; R6 = H, NMe2, 0Me, C0Me,
SMe, S0Me or S02Me; X = 0 or N0Me; or R1 + R2 is a bond; or R1 + R3 is CH2
or N = NCH2, in which case R2 = H; or R2 + R3 is CH2.
USE - (I) have progestational or antiprogestational activity and/or
antiglucocorticoid activity. They may be useful as antifertility agents
and in the treatment of Cushing's syndrome, ***glaucoma*** ,
endometriosia, premenstrual syndrome and cancer, and for oestrus
regulation in animals.
0/0
ABEQ US 4954490 A UPAB: 19930928
11beta-aryl-19-norprogesterone of formula (I) is new. R1 is OC(O)CH3,
OC(O)R5, where R5 is 2-8C-alkyl, -alkenyl, or -alkynyl or aryl, R2 is H;
R3 is H, 1-4C alkyl, 2-4C-alkenyl or -alkynyl; R4 is H, Me, F, Cl; R6 is
H, Me2N, MeO, Ac, MeS, MeSO, MeSO2; X is O, NOMe. Esp. cpds. include
17alpha-acetoxy-6alpha-methyl-11beta-(4-N,N-dimethylaminophenyl)-19-
norpregna-4,9- diene-3,20-dione. USE - These cpds. bind strongly to
progesterone and ***glucocorticoid*** ***receptors*** with
progestational, anti-progestational and anti-glucocorticoid activity, used
in treatment of cancer, and cushings syndrone and ***glaucoma*** . Unit
dose 0.1 mg-2g.
ABEQ US 5073548 A UPAB: 19930928
Beta-Aryl-19-norprogesterones of formula (I) are new. Where R1 = H, 1-4C
alkyl, 2-4C alkenyl, 2-4C alkynyl, OH, OCOMe or OCOR5, R5 = 2-8C alkyl,
2-8C alkenyl, 2-8C alkynyl or aryl, R2 = H; R3 = H, 1-4C alkyl, 2-4C
alkenyl or 2-4C alkynyl; R4 = H, Me, F or Cl; R6 = H, NMe2, OMe, COMe,
SMe, SOMe or SO2Me; X = 0 or NOMe, or R1 + R2 is a bond; or R1 + R3 is CH2
or N = NCH2, in which case R2 = H, or R2 + R3 is CH2.
USE - (I) have progestational or antiprogestational activity and/or
antiglucocorticoid activity. They may be useful as antifertility agents
and in the treatment of Cushing's syndrome, ***glaucoma*** ,
endometriosia, premenstrual syndrome and cancer, and for oestrus
regulation in animals.
ABEQ EP 422100 B UPAB: 19970410
An 11beta-phenyl-19-norprogesterone of the formula (I), wherein (i) (1) R1
is OC(OH)CH3 or OC(O)R5, wherein R5 is C2-8 alkyl, C2-8 alkenyl, C2-8

alkynyl or aryl, R2 is H, R3 is H, C1-4 alkyl, C2-4 alkenyl or C2-4
alkynyl, R4 is H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S,
CH3SO, CH3SO2, and X is O or NOCH3; or (i) (2) R1 is C2-4 alkenyl or C2-4
alkynyl, R2 is H, R3 is H, C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl, R4 is
H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO, CH3SO2, and X
is O or NOCH3; or (i) (3) R1 is C2-4 alkyl, R2 is H, R3 is H, C1-4 alkyl,
C2-4 alkenyl or C2-4 alkynyl, R4 is H, CH3, F or Cl, R6 is H, CH3CO, CH3O,
(CH3)2N, CH3S, CH3SO, CH3SO2, and X is O or NOCH3; or (i) (4) R1 is H or
C1-4 alkyl R2 is H, R3 is C2-4 alkyl, C2-4 alkenyl or C2-4 alkynyl, R4 is
H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO, CH3SO2, and X
is O or NOCH3; or (ii) R1 and R2 taken together are a carbon-carbon bond,
R3 is H, C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl, R4 is H, CH3, F or Cl,
R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO or CH3SO2, and X is O or NOCH3;
or (iii) R1 and R3 taken together are -CH2- or -N=N-CH2-, R2 is H, R4 is
H, CH3, F or Cl, R6 is H, (CH3)2N, CH3O, CH3CO, CH3S, CH3SO or CH3SO2, and
X is O or NOCH3; or (iv) R2 and R3 taken together are =CH2, R1 is H, C1-4
alkyl, C2-4 alkenyl or C2-4 alkynyl, R4 is H, CH3, F or Cl, R6 is H,
(CH3)2N, CH3O, CH3CO, CH3S, CH3SO or CH3SO2, and X is O or NOCH3.

Dwg.2/2

L6 ANSWER 32 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1988-091693 [13] WPIDS
DOC. NO. CPI: C1988-041156
TITLE: Steroid(s) having binding affinity for ***glucocorticoid*** ***receptor*** - are 17
alpha-substd-methyl-17 beta-hydroxy-steroid derivs .
DERWENT CLASS: B01 C03
INVENTOR(S): COOK, C E; REEL, J R, TALLENT, C R; WANI, M C; EDGAR, C, JERRY, R; TALLENT, C
PATENT ASSIGNEE(S): (RETR-N) RES TRIANGLE INST
COUNTRY COUNT: 11
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8801868	A	19880324 (198813)*	EN		45
RW: BE CH DE FR GB IT					
W: AU JP NL					
AU 8780208	A	19880407 (198827)			
US 4774236	A	19880927 (198841)			13
US 4861763	A	19890829 (198944)			11
CA 1327791	C	19940315 (199416)			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DATE
WO 8801868	A	WO 1987-US2303 19870915
US 4774236	A	US 1986-908288 19860917
US 4861763	A	US 1988-223873 19880725
CA 1327791	C	CA 1987-547105 19870917

PRIORITY APPLN. INFO: US 1986-908288 19860917; US 1988-223873 19880725
AN 1988-091693 [13] WPIDS
AB WO 8801868 A UPAB: 19930923
(1)Steroids having binding affinity for the ***glucocorticoid*** ***receptor*** and possessing glucocorticoid activity and of formula (I)
are new. Either the 1(2)-bond is single and the 9(10)-bond is double and A
is absent, or the 1(2)-bond is single or double, the 9(10)-bond is single
and A=Me; X = ethynyl, CN, N3, SCN, OMe or Ph; R = H or 1-5C acyl; R1 =
Me; R2 = (alpha H, beta OH) except when X = CN, or O; R3 = H. (2) In (I)
when there is 1,2-dihydro, and 4, 9(10) didehydro, then R1 may also be Et;
and R2 = alpha H, together with (CH2)nR5; R5 = pyridyl, thiazolyl, NMe2,
NEt2, 1-piperidinyl, 4-methyl-1-piperadinyl, OMe, C6H4R4; R4 = R5 or H,
O(CH2)2NMe2, O(CH2)2NEt2, 1-3C alkoxy, halogen, 1-3C alkylthio, 1-3C
alkylsulphinyl, Ph S or Ph SO; or (alpha H, beta CF3); (alpha H, beta
CHF2); = CHF or = CF2. Other combinations of substituents may be present.
USE/ADVANTAGE - (I) have glucocorticoid and antiglucocorticoid,
progestational and antiprogestational activities. Dose is 0.0001-1g/unit
dose.
/0
ABEQ US 4774236 A UPAB: 19930923
Glucocorticoid ***receptor*** -binding 17-alpha-(substd.
methyl)-17beta-hydroxy/esterified hydroxy steroids of formula (II) where Z
is of partial structure (III) or (IV), are new. In these formulae X is
-C=CH, CN, N3, SCN, OMe, Ph; R is Ac, propionyl, butyryl; R1 is Me; R2 is
alpha-H, beta-OH or =O provided that when X is CN, R2 is O; R3 is H.
USE - These steroids have glucocorticoid, anti-glucocorticoid, anti
-glucocorticoid, progestational and anti-progestational activity depending
on structure, having binding affinities to both types of receptor and are
used in treatment of inflammatory and allergic conditions,
glaucoma , stress and as contraceptive or estrogenic agents to
control fertility, and as antitumour agents. Dose e.g. 0.0001-1(0.001-1)g.
ABEQ US 4861763 A UPAB: 19930923
New steroids with binding affinity for the progesterone receptor and
having progestational activity are of formula (I) where X = CN, N3, SCN,
OMe or Ph opt. substd. by 1-3C alkyl. R = H or 1-5C acyl. R1 = methyl
or ethyl. R2 = alpha-H and beta-(1-3C alkyl); or alpha-H and beta-(2-4C
alkenyl); or methylene; or alpha-H and beta-p-fluorophenyl; or alpha-H
and beta-p-trifluoromethylphenyl; or alpha-H and beta-thienyl; and R3 = H
or methyl.

L6 ANSWER 33 OF 40 MEDLINE
DUPLICATE 8
ACCESSION NUMBER: 85233754 MEDLINE
DOCUMENT NUMBER: 85233754
TITLE: Cellular sensitivity to glucocorticoids in patients with
POAG. Steroid receptors and responses in cultured skin
fibroblasts.
AUTHOR: Polansky J, Palmberg P; Matulich D; Lan N; Hajek S; Hajek
A; Becker B; Baxter J
CONTRACT NUMBER: EY-01785 (NEI)
EY-01167 (NEI)
EY-02477 (NEI)
+
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1985 Jun)
26 (6) 805-9.
Journal code: GWI. ISSN: 0146-0404.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198510
AB The question of a generalized hypersensitivity to corticosteroids in
primary open-angle ***glaucoma*** (POAG) was investigated using
cultured skin fibroblasts from patients with POAG and age-matched
controls. Nuclear binding of (3H)-dexamethasone was performed to evaluate
possible changes in the ***glucocorticoid*** ***receptors***.
Cortisol effects on (3H)-thymidine uptake into the cells were investigated
as a measure of the cellular sensitivity to corticosteroids. When POAG and
control groups were compared, no significant differences (P less than
0.05) were found for either the number or affinity of ***glucocorticoid*** ***receptors*** (POAG: Kd = 6.1 +/- 1.0 nM, Rt
= 94 +/- 13 sites/cell X 10(3); control: Kd = 5.5 +/- 1.6 nM, Rt = 124 +/-
20 X 10(3) sites/cell) or for cortisol effects on thymidine uptake (POAG:
C50 = 83 +/- 38 nM; control: C50 = 80 +/- 34 nM). Use of epidermal growth
factor (EGF) resulted in an increased steroid sensitivity in some cell
lines, but again no differences between POAG and control groups were
detected. These results suggest that a generalized cellular
hypersensitivity to glucocorticoids is not intrinsic to POAG. It is
possible that environmental alterations and/or endogenous factors may
influence the steroid responses observed in these patients.

L6 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 9
ACCESSION NUMBER: 1984:62502 CAPLUS
DOCUMENT NUMBER: 100:62502
TITLE: Prostaglandin production by human trabecular cells:
in vitro inhibition by dexamethasone
AUTHOR(S): Weinreb, Robert N.; Mitchell, Murray D.; Polansky, Jon R.
CORPORATE SOURCE: Med. Cent., Univ. California, San Francisco, CA, USA
SOURCE: Invest. Ophthalmol. Visual Sci. (1983), 24(12), 1541-5
CODEN: IOVSDA; ISSN: 0146-0404
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Morphol. differentiated human trabecular cells produced high levels of
PGE2 [363-24-6] and somewhat lower levels of PGF2.alpha. [551-11-1], and
6-keto-PGF1.alpha. (6KF1.alpha.) [58962-34-8] in the presence and absence
of serum. In a typical expt., the following PG levels were detected in
the cell culture media after 24 h: PGE2, 225; PGF2.alpha., 33.5;
6KF1.alpha., 12.7 ng/mL in the presence of 10% fetal calf serum; and PGE2,
30.0; PGF2.alpha., 4.8; 6KF1.alpha., 3.6 ng/mL in serum-free media.
Moderate concns. of dexamethasone (DEX) [50-02-2] decreased the levels of
all 3 PGs. For PGE2 prodn., 10-8M DEX inhibited .apprx.75%, and 10-7M DEX
inhibited .apprx.90%. The IC50 for inhibition of PG prodn. by DEX was <10
nM, thus indicating that the steroid effect probably involved
high-affinity ***glucocorticoid*** ***receptors***. These
findings emphasize the possibility that physiol. levels of glucocorticoids
may regulate PG prodn. within the meshwork, and suggest that studies of

endogenous PG prodn. by trabecular cells could provide new clues to the pathogenesis of a no. of ***glaucoma*** syndromes, including primary open-angle ***glaucoma*** and steroid ***glaucoma***

L6 ANSWER 35 OF 40 MEDLINE
DUPLICATE 10
ACCESSION NUMBER: 84017537 MEDLINE
DOCUMENT NUMBER: 84017537
TITLE: Potentiation of glucocorticoid activity by 5 beta-dihydrocortisol: its role in ***glaucoma***
AUTHOR: Weinstein B I; Gordon G G; Southren A L
CONTRACT NUMBER: EY 01313 (NEI)
SOURCE: SCIENCE, (1983 Oct 14) 222 (4620) 172-3.
Journal code: UJ7 ISSN: 0036-8075
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198401
AB 5 beta-Dihydrocortisol potentiated the threshold level (the smallest dose producing a measurable effect) of topically applied cortisol (0.02 percent) and dexamethasone (0.003 percent) in causing nuclear translocation of the cytosolic ***glucocorticoid*** ***receptor*** in rabbit iris-ciliary body tissue. 5 beta-Dihydrocortisol accumulates in cells cultured from trabecular meshwork specimens from patients with primary open-angle ***glaucoma*** , but not in similar cells derived from nonglaucomatous patients. In view of the sensitivity of patients with primary open-angle ***glaucoma*** to the effects of glucocorticoids in raising intraocular pressure, this potentiation may be responsible for the steroid sensitivity and for the ocular hypertension seen in this disorder.

L6 ANSWER 36 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 82107525 EMBASE
DOCUMENT NUMBER: 1982107525
TITLE: Radioautography of dexamethasone in human eye tissues. A preliminary report.
AUTHOR: Tchernitchin A.N.; Tchernitchin N.; Anguita-Salas J.; et al.
CORPORATE SOURCE: Dept. Exp. Morphol., Lab. Exp. Endocrinol., J.J. Aguirre Hosp., Univ. Chile Med. Sch., Santiago, Chile
SOURCE: IRCS Medical Science, (1982) 10/3 (257).
CODEN: IRLCDZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
023 Nuclear Medicine
012 Ophthalmology
LANGUAGE: English
AB Glucocorticoid administration increases intraocular pressure in rabbits and humans. In the rabbit eye, radioautographic studies have localized ***glucocorticoid*** ***receptors*** in the aqueous production, suggesting their involvement in the pathogenesis of glucocorticoid-induced ***glaucoma*** . Human eye tissue from 5 patients with open-angle ***glaucoma*** was obtained from trabeculectomy, incubated with tritiated dexamethasone, and submitted to the dry radioautographic technique for diffusable compounds. Radioautograms revealed nuclear labeling in stromal and endothelial cells from the trabecular meshwork, scleral spur, the anterior face of ciliary body and iris root. The similarities between radioautographic findings in the rabbit and in the human eye suggests that the previously proposed hypothesis for the pathogenesis of glucocorticoid-induced increase in intraocular pressure in the rabbit may well be valid for the human eye.

L6 ANSWER 37 OF 40 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1981-83483D [45] WPIDS
TITLE: Irreversible inhibition of glucocorticoid activity in subject - by admin. of cortisol or dexamethasone 21-mesylate(s).
DERWENT CLASS: B01
INVENTOR(S): SIMONS, S S
PATENT ASSIGNEE(S): (USGO) US GOVERNMENT
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 4296206	A	19811020	(198145)*		9

PRIORITY APPLN. INFO: US 1980-145350 19800430
AN 1981-83483D [45] WPIDS
AB US 4296206 A UPAB: 19930915
Inhibition of glucocorticoid action in a subject comprises admin. of cortisol 21-mesylate (I) or dexamethasone 21-mesylate (II).
Cpds. (I) and (II) are irreversible antiglucocorticoids; they have a low but significant cell-free affinity for the ***glucocorticoid*** ***receptors*** of rat hepatoma tissue culture cells and they inhibit tyrosine aminotransferase (TAT) induction in the cells. This inhibition of TAT is not due to cell toxicity. Cpds. (I) and (II) are the first known irreversible antiglucocorticoids, possibly because they form covalent receptor-steroid complexes.
Cpds. (I) and (II) may be used for blocking glucocorticoids in the treatment of non-operable hyperglucocorticoid syndromes esp. adrenal carcinomas and ectopic ACTH syndrome. Patients who can be treated are those hyper-responsive to glucocorticoids, e.g. with open-angle ***glaucoma*** or those who are homozygous for the postulated gene defect causing this disease, with blocking some of the steroids and thus attenuating responses in sensitive cells. Cpds. (I) and (II) can also be used for pre-operative treatment of patients with Cushing's disease to eliminate the complications of surgery due to elevated glucocorticoid levels. They are also useful in studies of the mechanism of glucocorticoid hormone action; irreversible glucocorticoid activity is shown at 10 to minus 9 to 10 to minus 5 M.

L6 ANSWER 38 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 81237418 EMBASE
DOCUMENT NUMBER: 1981237418
TITLE: Autoradiography of 3H-dexamethasone following topical ophthalmic administration.
AUTHOR: Tchernitchin N., Anguita-Salas J., Canas-Kramarosky M.M.; et al.
CORPORATE SOURCE: Lab. Exp. Endocrinol., Dept. Exp. Morphol., J.J. Aguirre Hosp., Univ. Chile Med. Sch., Santiago, Chile
SOURCE: IRCS Medical Science, (1981) 9/9 (887-888).
CODEN: IRLCDZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 012 Ophthalmology
023 Nuclear Medicine
037 Drug Literature Index
LANGUAGE: English
AB Previous results have shown ***glucocorticoid*** ***receptors*** in cells related to aqueous humor outflow, but not in cells related to its production, suggesting an explanation for the pathogenesis of glucocorticoid-induced ***glaucoma*** . Ophthalmic glucocorticoids administered topically are widely used. This study describes local and systemic diffusion and localization of 3H-dexamethasone after topical ophthalmic administration in rabbits, using dry radioautography for diffusible compounds. Nuclear concentration of radioactivity is found in the same cell-types which have been proposed to be involved in the glaucomatous response; in addition, it was found in some extraocular target cells. This nuclear concentration of label is not observed in animals pretreated with excess of unlabeled dexamethasone, strongly suggesting competition and saturation of receptors. This study provides an explanation for the glaucomatous response that follows topical treatment with ophthalmic glucocorticoids, and alerts to the possibility of systemic dangerous effects.

L6 ANSWER 39 OF 40 MEDLINE
DUPLICATE 11
ACCESSION NUMBER: 82006886 MEDLINE
DOCUMENT NUMBER: 82006886
TITLE: Detection of ***glucocorticoid*** ***receptors*** in cultured human trabecular cells.
AUTHOR: Weinreb R N, Bloom E, Baxter J D, Alvarado J, Lan N, O'Donnell J, Polansky J R
CONTRACT NUMBER: EY02477 (NEI)
EY01785 (NEI)
EY02162 (NEI)
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1981 Sep)
21 (3) 403-7.
Journal code: GWI. ISSN: 0146-0404.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198201
AB To evaluate potential direct effects of glucocorticoids on the aqueous outflow pathway, the cellular binding of steroids to cultured human trabecular cells was examined. After incubation of cells with 5 to 40 nM [3H]dexamethasone, specific binding (i.e., binding that could be blocked by an excess of nonlabeled steroid) was detected by measuring the total cell-associated labeled hormone. A binding affinity of 5 nM and 60,000 receptor sites/cell were demonstrated with labeled dexamethasone. Incubation of human trabecular cells with 40 nM [3H]dexamethasone for 60 min revealed that 62% +/- 7 of the specific binding

was found in the
nuclear fraction and 38% +/- 3 was in the cytoplasmic fraction. In
competition studies, dexamethasone had a higher affinity for these sites
than cortisol, which in turn had a higher affinity than progesterone.
These studies suggest that functional ***glucocorticoid***
receptors are present in human trabecular cell cultures. Therefore
it is possible that a direct action of glucocorticoids on trabecular cells
could contribute to the decreased outflow facility observed in steroid
glaucoma

L6 ANSWER 40 OF 40 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 78318236 EMBASE
DOCUMENT NUMBER: 1978318236
TITLE: ***Glucocorticoid*** ***receptors*** in primary open-angle ***glaucoma*** .
AUTHOR: Palmberg P.; Becker B.
CORPORATE SOURCE: Washington Univ. Sch. Med., St Louis, Mo., United States
SOURCE: Investigative Ophthalmology and Visual Science, (1978) 17/Suppl. (208).
CODEN: IOVSDA
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English